OVERWEIGHT AND OBESITY: EPIGENETICS, SOCIO-DEMOGRAPHIC, ENVIRONMENTAL, AND LIFESTYLE RISK FACTORS AMONG U.S. ADULTS

A Dissertation

by

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ABSTRACT

Obesity and overweight have become national health concerns and have contributed to many non-communicable or chronic diseases such as type 2 diabetes (T2D), cardiovascular complications, and cancers. A variety of factors, including demographic, genetic, lifestyle, environmental, and socioeconomic factors, are considered determinants for obesity and overweight, suggesting the complexity of the issue. Yet, most studies thus far have focused on the linear and isolated effects of individual factors, ignoring the complex interconnectivity between obesity/overweight and these factors. Similarly, existing health education and intervention programs primarily follow a piecemeal approach to address the obesity and overweight challenge, thus meeting with only limited success.

The objectives of this study, therefore, are to: 1) assess the role of epigenetics in the obesity and overweight epidemic based on a review and synthesis of recent advances in epigenetics and genetics; and 2) statistically assess the relationship(s) between weight status and a set of socio-demographic, lifestyle, and environmental factors (SDLEFs) considered simultaneously, among the U.S. adult population.

The emergence of epigenetics and recent developments in genetics, genomics, and epigenetics suggest that genetic factors alone account for only a small part of the overweight and obesity epidemic and that epigenetics can play a vital role in explaining and curbing obesity and overweight risk. Unlike genetics, which focuses — as a field of study — on DNA coding sequences (genes) and underlying gene functions, epigenetics

unveils dynamic gene-environment interactions. Empirical evidence also supports the claim that epigenetic factors play an important role in overweight and obesity.

Multinomial logistic regression analyses of the 2012 National Health Interview Survey (NHIS) data were employed to estimate the relationships between overweight or obesity and SDLEFs. Body Mass Index (BMI) was used to define normal weight (18.5 $kg/m^2 \leq BMI < 24.9\ kg/m^2$), overweight ($25\ kg/m^2 \leq BMI < 29.9\ kg/m^2$), and obesity ($BMI \geq 30\ kg/m^2$). The SDLEFs considered include age, gender, race, marital status, smoking, alcohol consumption, physical activity, hours of sleep, and geographic region.

Results highlight the nonlinear relationships between BMI and the SDLEFs and the joint effects of SDLEFs on BMI. There are large gender and racial differences in the risk for overweight and obesity. Females are more likely to be overweight and obese than males, and Asian Americans are less likely to be overweight and obese than any other racial group. Additionally, strength-training physical activity is more effective in reducing the risk of overweight and obesity than moderate and vigorous physical activity. The regression results confirm the importance of an epigenetic approach to obesity and overweight.

This study sheds new light on the potential for epigenetics to help health educators and public health professionals understand and leverage the linkages between SDLEFs and overweight/obesity, when developing intervention or prevention programs. This study's findings can help inform future health research, education, and intervention programs to mitigate the overweight/obesity epidemic. They also suggest implications for future health education/health promotion degree programs' foci and curricula.

DEDICATION

To my beloved father and mother

and

My heavenly Father, everlasting God.

To my best friend and my beloved husband

Jianbang Gan

for his constant support and true love.

To my sons—Steven, Eric, and David—

you all are truly my inspiration and blessings!

This dissertation is dedicated to my dad who was a life-long educator, servant of the Lord, a deacon of his local village church in China, and who always had a vision for his daughters to pursue education and personal happiness; to my mom who was truly an amazing woman and always inspired me with her wisdom, unconditional love, caring, and kindness; to my darling husband Jianbang (Jim) who is my true love and best friend; to my sons Steven, Eric, and David who have made me a proud mom. You all have made me proud. You all have been my power source and helped me to be a better daughter, wife, mother, and human being. Without the love of you all, I could never have done it.

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1. INTRODUCTION

> "People often have this sense of genetic determinism — that they are nothing but their genes. Those genes contain their destiny written in the DNA. This is nonsense. We know that there is a tremendous influence of environment, of society, on outcome. If you just think about the fact that the human gene pool hasn't significantly changed in the last 5,000 years, and you realize that our genes really can't determine things. They can be influences, but for the longest time … people looked to the genome to justify their prejudices about what people could or couldn't do." — Eric Lander (PBS, 2001, NOVA online interview).

Obesity and overweight are a national public health issue in the United States. The prevalence of obesity in the last few decades has become an unprecedented challenge, threatening public health, increasing medical expenditures, and potentially weakening the nation's productivity, prosperity, and security, in the long run. The overweight/obesity problem has become increasingly severe in recent years and across almost all ages, gender, and racial/ethnic groups. National health statistics reveal that over 1/3 of U.S. adults are currently obese and have a body mass index (BMI) greater than 30 kg/m^2; the other 1/3 of U.S. adults are overweight (with a BMI between 25 kg/m^2 and 30 kg/m^2) (National Center for Health Statistics, 2017). The concern about overweight and obesity is prevalent not only among civilians but also in the U.S.

military (Eilerman et al., 2014). Together, more than 2/3 of Americans are either overweight or obese (National Center for Health Statistics, 2017).

These overwhelming obesity and overweight rates are in the opposite direction of the Healthy People 2020's goal: "All Americans should avoid unhealthy weight gain, and those whose weight is too high may also need to lose weight" (HealthyPeople.gov, n.d., para. 5). Obesity impacts not only individuals, families, communities, and our nation at the present time, but also future generations. Some researchers have predicted that current obese children in the U.S. will be the first generation to have a shorter lifespan than their parents and grandparents since industrialization (Daniels, 2006; Mann, 2005; Olshansky et al., 2005).

Overweight and obesity are closely associated with the development of chronic diseases such as type 2 diabetes (T2D), high blood pressure, unhealthy cholesterol levels, heart disease, stroke, osteoporosis, asthma, sleep apnea, gallbladder and kidney stones, infertility, and eleven types of cancers (Kopelman, 2000 & 2007; Mokdad et al., 2003; Reilly et al., 2003; Wyatt, Winters, & Dubbert, 2006). Obese individuals might also experience social, emotional, psychological, and behavioral difficulties (Cahnman, 1968; Friedman & Brownell, 1995; Hill, 2008; Jeffery, French, Forster, & Spry, 1991; Strauss, Smith, Frame, & Forehand, 1985) including discrimination (low wages, unemployment) (Carr & Friedman, 2005; Puhl & Brownell, 2001; Rand & Macgregor, 1990), poor quality of life (Larsson, Karlsson, & Sullivan, 2002; Zeller & Modi, 2006), and depression (Leckie & Withers, 1967; Luppino et al., 2010; Stunkard, Faith, & Allison, 2003).

If current trends continue, there will be roughly 32 million obese adults in the U.S. by the year 2030, costing approximately $550 billion in medical expenses between now and then (Finkelstein, Trogdon, Cohen, & Dietz, 2009). The economic burden of obesity in 2008 alone was $147 billion for medical costs and $60 billion for non-medical costs related to weight control (Finkelstein et al., 2009). Obesity and its health complications have claimed 30,000 premature deaths each year and are the second leading cause of death after tobacco smoking in the U.S. (Mokdad et al., 2001). With the gradual decline in smoking, obesity will become the leading cause of death in the next few years; apart from tobacco, currently there is no greater harm to public health in the U.S. than obesity (Mokdad et al., 2001).

What is the primary factor influencing obesity — genetic inheritance, environment/lifestyle, or both? Since the completion of the Human Genome project (International Human Genome Sequencing Consortium, 2004), scientists have focused on a genetic variance approach to identifying BMI-associated genes. They rely on candidate genes and on a whole human genome-wide association study (GWAS) approach to identify single nucleotide polymorphisms (SNP) genetic loci responsible for obesity. To date, more than 30 genetic loci associated with BMI have been identified (Pérusse et al., 2005; Speliotes et al., 2010). Surprisingly, these 30 loci account for only 1.5% of individual variations in BMI (Ochner, Tsai, Kushner, & Wadden, 2015). The GWAS genomic research, on the other hand, has also pointed to the possibility of environmental and lifestyle factors influencing BMI gene function, or the so called

"gene-environment interaction" (Harvard School of Public Health, 2017; Marti, Martinez-González, & Martinez, 2008).

Although tremendous efforts — including heath education, health promotion, and medical treatments — have been attempted to solve the overweight and obesity crisis, these efforts have met with only limited success so far (Baskin, Ard, Franklin, & Allison, 2005; Chan & Woo, 2010; Roberto et al., 2015; Wang et al., 2013). Several reasons may explain such lack of success. First, obesity and overweight are a complex, dynamic problem (Mokdad et al., 2001; Roberto et al., 2015). Many factors contribute, jointly, to obesity and overweight (Chan & Woo, 2010; Keith et al., 2006). Second, much of the current research focuses primarily on isolated effects of individual factors and, almost exclusively, on linear relationships between obesity/overweight and determining factors (Chan & Woo, 2010; Miller, Koceja, & Hamilton, 1997). Moreover, studies tend to lack multi- or transdisciplinary approaches (Chan & Woo, 2010). Third, existing health education and intervention programs are also narrowly focused on obesity/overweight in terms of both their scope and their dynamics (Flynn et al., 2006; Miller et al., 1997). Furthermore, often due to funding and other constraints, these programs tend to follow piecemeal and fragmented approaches (Flynn et al., 2006; Roberto et al., 2015; Wang et al., 2013). To enhance the efficacy of efforts to prevent and control obesity and overweight, much work is still needed in research, education, prevention, and treatment (Roberto et al., 2015; Wu et al., 2013).

Against this backdrop, the long-term goal of this study is to provide a novel perspective for developing effective health education and intervention approaches to

mitigate overweight and obesity risk among the U.S. adult population. To reach this goal, this study aims to achieve the following four specific objectives:

1) To review recent advances in epigenetics as related to overweight and obesity;
2) To discuss the potential for and approaches to incorporating epigenetic principles and mechanisms into health education and interventions to mitigate the overweight and obesity crisis;
3) To identify socio-demographic, environmental, and lifestyle factors (SDELFs) associated with overweight and obesity among a nationally representative sample of adults in the U.S.; and
4) To assess the nonlinear statistical association among socio-demographic, lifestyle, environmental factors and overweight and obesity risk among the U.S. adult population.

To achieve the above objectives this study comprises two units, presented in Chapters 2 and 3, respectively. The first unit (Chapter 2) consists of a review and theoretical treatment of the recent advances in epigenetics and how these advances can help health educators/health promoters better understand the mechanisms linking various environmental and lifestyle factors to obesity/overweight. The second unit (Chapter 3) will examine the socio-demographic, lifestyle, and environment factors that are nonlinearly associated with overweight/obesity among a representative sample of adults in the U.S. This assessment will support the claim that epigenetic mechanisms can

provide a better understanding of the relationship between SDELFs and obesity/overweight.

This dissertation is organized, therefore, into four chapters. Following this chapter providing a general introduction, Chapter 2 contains the review and theoretical treatment of advances in epigenetics and their potential applications to health education and health promotion. Chapter 3 reports on the statistical analyses of the nonlinear relationships between a set of socio-demographic, lifestyle, and environmental factors, and overweight/obesity risk. Finally, Chapter 4 synthesizes key findings and overall conclusions based on previous chapters.

2. INCORPORATING AN EPIGENETICS APPROACH INTO HEALTH EDUCATION AND INTERVENTIONS TO ADDRESS OVERWEIGHT AND OBESITY

2.1 Obesity, genetics and epigenetics

2.1.1 The obesity problem in the U.S.

In a few short decades, the adult obesity rate in the U.S. has tripled and the obesity rate for children aged between 2 and 19 has doubled — with accompanying costs for health care and productivity loss of the U.S. workforce (Baskin et al. 2005; National Center for Health Statistics, 2017; Ogden, Carroll, Curtin, Lamb, & Flegal, 2010; Ogden et al., 2006; Wang, Beydoun, Liang, Caballero, & Kumanyika, 2008). If the current trend continues, by the year 2030 the adult obesity rate could reach 51.1% in the U.S. (Wang et al., 2008). In 2008, our nation spent more than $147 billion to care for obesity and obesity-related health complications which are preventable (by spending 50% less), including heart disease and diabetes (Cawley & Meyerhoefer, 2012). In recent years, annual medical costs for treating obesity-related health complications in the U.S. are estimated at $3,115 per adult and account for 16.5% of total national health expenditures (Cawley & Meyerhoefer, 2012). Compared with healthy, normal weight individuals, obese adults spend 42% more on direct medical care (Finkelstein et al., 2009).

The ineffectiveness of existing obesity intervention programs (Baskin et al., 2005; Chan & Woo, 2010; Ogden et al., 2001; Wang et al., 2013) is partially attributable to the ignorance or lack of understanding of the association between environmental

changes and physiological mechanisms, including epigenetic effects, responsible for shaping obesity (Keith et al., 2006; Saugstad, 2004). Many studies have found that epigenetic factors rather than genetic factors have contributed significantly to obesity and overweight (Heitmann et al., 2012; Jackson, Niculescu, & Jackson, 2013; Keith et al., 2006; McAllister et al., 2009; Milagro, Mansego, de Miguel, & Martinez, 2013; Mustard, 2010). Yet, these important findings in epigenetics have not been incorporated into the majority of obesity intervention and education programs for humans, despite demonstrated benefits in animal studies (Heitmann et al., 2012; Milagro et al., 2013; Saugstad, 2004). Therefore, it is critical for health educators, public health practitioners, and health care professionals to understand epigenetic causes of overweight and obesity and adopt epigenetic principles in obesity prevention and education.

2.1.2 Epigenetics and obesity

Epigenetics aims to understand how environmental factors influence gene expression impacting individual phenotypic variation and susceptibility to complex health conditions and diseases including overweight and obesity (Cho & Blaser, 2012; Handel, Ebers, & Ramagopalan, 2010; Uauy, Albala, & Kain, 2001). To date, three known epigenetic mechanisms including DNA (deoxyribonucleic acid) methylation, histone acetylation, and non-coding or small RNA (ribonucleic acid) have been linked to epigenetic changes in gene expression and function (the definitions of these epigenetic mechanisms will be explained later in Section 2.1.5).

The epigenetic changes in gene expression and function act like a switch and can turn a gene "on" or "off." Growing evidence suggests that DNA methylation, histone, and non-coding RNA are also influenced by environmental factors and can turn a gene "on" or "off" (Dolinoy, Huang, & Jirtle, 2007; Weinhold, 2006). There is increasing evidence that DNA methylation is a crucial epigenetic modification of the genome associated with gene silencing (the "turning off" of gene/genes) (Baylin, 2005; Robertson, 2005) and that histone acetylation (Schübeler et al., 2004; Wang et al., 2008) and non-coding or small RNA (Rinn et al., 2007; Wang et al., 2011) are linked to gene expression (the "turning on" of gene/genes). However, researchers are still exploring what environmental and lifestyle factors might cause these epigenetic changes that alter gene expression or gene silencing.

Turning genes "on" or "off" via epigenetic mechanisms is mainly influenced by non-genetic external factors (external to the gene) — during the course of life (Daxinger & Whitelaw, 2012; Jirtle & Skinner, 2007; Rutter, 2012). For example, obesity researchers have been exploring how epigenetic change mechanisms might "turn on" adiposity genes instead of "turning them off;" or how they may "turn off" the lean skeletal-muscle genes instead of "turning them on." Understanding which factors cause epigenetic change mechanisms could lead to more effective health interventions, prevention, or even a treatment which might offer cure for overweight and obesity for future generations.

Previous research shows that epigenetic changes impact the current generation's gene expression throughout the course of the life of an organism. Additionally,

increasing evidence indicates epigenetic changes caused by the environment do not disappear during the embryonic and gamic development stages and can be inherited (Bjornsson, Fallin, & Feinberg, 2004). From human to animal model studies, researchers have demonstrated that epigenetic changes can pass onto the subsequent generations (Angers, Castonguay, & Massicotte, 2010; Bond & Finnegan, 2007; Dunn & Bale, 2011). Many studies have indicated that epigenetic alterations can affect up to three or four generations if under a similar environment and life experiences. For example, studies have found a link between a current generation's weight status and the previous generation's environment and life experiences. These environmental factors include climate, air quality, living environment, and environmental toxins, while the lifestyle factors comprise diet, macro and micro nutrition, age of smoking initiation, alcohol consumption status, family, work related stress, sleep depletion, physical activity, and weigh status (Alegría-Torres, Baccarelli, & Bollati, 2011; Dunn & Bale, 2011).

Scientists have determined that epigenetic effects impact reproductive cells (eggs and sperms) across three generations. For example, studies have found that the weight status prior to pregnancy, nutrition, diet, and stress might be directly linked to epigenetic changes in gene function in the subsequent generations (Barouki, Gluckman, Grandjean, Hanson, & Heindel, 2012; Dunn & Bale, 2011). In the case of the well documented Dutch famine winter between 1944 and 1945 (Stein, Susser, Saenger, & Marolla, 1975), the babies conceived during that winter were found to have significantly higher obesity, diabetes, and cardiovascular disease rates than their siblings conceived post-famine.

Two generations later, their grandchildren had higher rates of chronic diseases associated with metabolic syndromes such as overweight/obesity (Scholte, van den Berg, & Lindeboom, 2015), diabetes (Kahn, Graff, Stein, & Lumey, 2008), cardiovascular and heart diseases (Lumey, Stein, Kahn, & Romijn, 2009; Lumey & van Poppel, 1994; Scholte et al., 2015; Stein & Lumey, 2000), personality disorders (Neugebauer, Hoek, & Susser, 1999), and negative health status in later life (Kesternich, Siflinger, Smith, & Winter, 2015) compared to their siblings conceived post-famine. The famine environment of that time (e.g., caloric restriction, hunger episodes, and harsh environment) caused the epigenetic changes responsible for these outcomes. This is a perfect but tragic example indicating that epigenetic changes play a role in these adverse outcomes.

2.1.3 Genetic view of overweight and obesity

What is a gene?

A gene is the basic physical and functional unit of heredity. It is a segment of DNA, the molecule that stores the code for building living organisms. In other words, a gene is a single unit of genetic information, stored on twisting double helix strands in every cell of every living being (Gerstein et al., 2007).

There are between 20,000 and 25,000 genes in humans, and over 99% of genes are the same between people (National Institute of Health, 2017a). The parents' genes combine to make the child's genes (one set of genes from the mother and the other set of

genes from the father). Genes control the color of some discrete traits (color of eyes, hair, and skin as well as some unique personalities).

What is genetics? How is it different from epigenetics?

Genetics as a field of knowledge focuses on DNA coding sequences, genes, and underlying gene functions. For example, scientists use the term "genetics" to refer to how DNA sequences lead to changes in the cell within the host. In turn, "epigenetics," as another field of knowledge, focuses on how DNA or genes are regulated to achieve those changes through gene expression and gene regulation. Without knowing the basics of genetics it can be difficult to understand epigenetics and how epigenetic changes can alter gene regulation and expression with known tags and mechanisms. The field of Genetics also includes the construct of Genomics, which refers to the whole DNA sequence present within one cell of an organism.

Genetic information is encoded in the underlying DNA sequence. Gene function is expressed through transcription from DNA to RNA then to development of proteins, a process known as the "central dogma" (DNA-RNA-Proteins) (U.S. National Library of Medicine, 2017). Genetic heredity explains how genetic traits pass on from one generation to the next, and how much genetic information is different or similar across organisms. The most important part of genetics is dealing with how gene mutations lead to genetic diseases and how to overcome and prevent genetic disorders (National Institute of Health, 2017b).

DNA and RNA are made of building blocks called nucleotides, a group of compounds consisting of a nucleoside combined with a phosphate group. There are four nucleotides (A, T, C, G) in DNA and four nucleotides (A, U, C, G) in RNA. For RNA, the Uracil (U) replaces the Tyrosine (T) in DNA. However, not all DNA sequences are coded for functional genes. If DNA sequences are coded for non-functional genes, they are also referred to as a "gene desert" (National Institute of Health, 2017b).

Role of genetics in overweight and obesity

A genetic sequence is consistently passed from one generation to the next with miniscule variations. Any two random individuals share 99% of identical DNA sequences (National Institute of Health, 2017a). Even though monozygotic twins share identical DNA and genetic information associated with genes, one of the twins may be overweight/obese, and the other twin may be thin or underweight. The babies conceived during the Dutch Hunger Winter in the example previously mentioned (Stein et al., 1975) had a higher obesity rate compared to their younger siblings (Kahn et al., 2008; Kesternich et al., 2015; Lumey et al., 2009), revealing genetics cannot fully explain the cause of obesity and overweight. Furthermore, studies have also confirmed that among identical genetically inbred mice (siblings), some have brown coats (phenotypically are lean and muscular), but others have yellow coated fur and are obese or prone to obesity related diseases (Dolinoy, Weidman, Waterland, & Jirtle, 2006; Dolinoy, Weidman, & Jirtle, 2007).

If overweight and obesity were fully caused or explained by genes, then there would not be much that health educators and public health professionals could do to alleviate the obesity epidemic. Health interventions or health promotion programs aimed to change diet, increase physical activity, enhance social equality, and promote healthy behavior changes are not able to change people's DNA or genes. The human genome or DNA remains unchanged after the zygomatic and embryo stage, unless a mutation occurs during development.

Scholars have determined that genetics (loci) account for less than 2% of the inter-individual BMI variation for monogenic (single gene) overweight and obesity susceptibility (Herrera, Keildson, & Lindgren, 2011; Lindgren et al., 2009). The genomic sequence of an individual is not going to change much except for random mutations of certain genes. A mutation is any alteration of the nucleotide sequence (A, C, T, G) of a genome which includes substitutions, insertions, and deletions. To date, studies published in the journal Nature using next-generation sequencing (which provides the most accurate human mutations passed from one generation to the next) reveal 100-200 mutations of the Y chromosome per generation (Dolgin, 2009). According to the information gathered since the completion of the human genome sequencing, mutations happen at a rate of approximately 10^{-8} per base pair (bp) per generation. If a normal human cell multiplies approximately 100 replications per generation, then it yields approximately 0.1 to 1 mutation per genome per replication (Sachidanandam et al., 2001). The whole human genome is about $3x10^{9}$ base pairs per genome, and multiplying by a mutation rate of 10^{-8} then yields about 10~100 mutations

per *generation* (BNID110293) (Dolgin, 2009). Additionally, the internal DNA repairing, proof reading, and cell cycle checking point mechanisms are also able to catch some mistakes in the early stages and eliminate certain mutations.

Basically, heritable genetic information coded in underlying DNA sequences being transcribed or copied precisely from a previous generation into the next has a meager mutation rate. In contrast to this minute mutation rate, however, the overweight and obesity rates have increased exponentially in the last few decades. Increasing evidence demonstrates that genetics plays a *very small role* in the current obesity crisis (Herrera & Lindgren, 2010; Lindgren et al., 2009; Saunders, 2007). Despite this established fact, billions of dollars have been spent on searching for genes responsible for obesity and diabetes. To date, over 150 loci (specific genes/places in the genome) have been discovered linked to obesity and diabetes and 30 loci have been associated with body mass index (BMI) (Herrera & Lindgren, 2010; Lindgren et al., 2009). However, in tandem, these loci explain less than 5% of cases of obesity and diabetes, and less than 2% of BMI-associated health issues (Herrera & Lindgren, 2010; Lindgren et al., 2009).

Genetics and genomics have been the focus of attention in searching for causes of, and solutions to obesity and overweight for a long time. However, the genetic view of overweight and obesity has very limited applications to either maintaining weight loss or preventing further weight gain. Genes alone cannot fully account for the obesity epidemic. Other factors besides genetics must also be at play.

2.1.4 Epigenetic view of overweight and obesity

What is epigenetics?

In the word epigenetics, the "epi" prefix comes from the Greek, meaning "above," "over," or "before;" thus, epigenetics simply means "above genetics" (Riddihough & Zahn, 2010). While epigenetics also focuses on genes and their "behaviors," compared to genetics, epigenetics as a field focuses more narrowly on gene regulation through the controlling of gene expression. Epigenetics tries to answer questions such as, how does the cell "turn on" or "turn off" genes? How does the gene-environment interaction take place without changing the underlying DNA sequence? How does gene expression (activity of the genes that produce proteins) change in response to environmental cues (Bird, 2007; Dolinoy, Huang, & Jirtle, 2007; Weinhold, 2006)?

Role of epigenetics in overweight and obesity

The epigenetic view of overweight and obesity links genes with non-genetic factors (external unhealthy environmental factors, such as sedentary lifestyle, poor dietary habits) as causes for developing obesity phenotypic variation without changes in the underlying DNA sequences. In other words, the epigenetic view of overweight and obesity links nature to nurture (or genes to their environmental interactions) (Campion, Milagro, & Martinez, 2009; Cooney, Dave, & Wolff, 2002; Richards, 2006). Negative environmental and lifestyle factors may increase the susceptibility to developing overweight and obesity, especially for individuals who have a family history of

overweight/obesity or higher BMI-related gene mutations (Ajslev, Ängquist, Silventoinen, Baker, & Sørensen, 2014; Møller, Ajslev, Andersen, Dalgård, & Sørensen, 2014). However, increasingly, studies from animal models reveal that positive environmental and lifestyle factors also can *reverse* the susceptibility to developing overweight/obese. Animal model studies indicate that epigenetic mechanisms associated with environmental and lifestyle factors can function in either direction (Dolinoy et al., 2006; Waterland, Travisano, & Tahiliani, 2007).

Emerging findings in epigenetics connect nature to nurture, a connection that has been largely ignored in the era of modern genomics (Reddon, Guéant, & Meyre, 2016). Applying both epigenetic and genetic approaches to obesity as well as to obesity-related chronic disease treatments and prevention can be significant because epigenetic change mechanisms offer hope not only for obesity treatment but also for its prevention among future generations (Barisione, Carlini, Gradaschi, Camerini, & Adami, 2012; Kappil, Wright, & Sanders, 2016). Therefore, it is important for health educators and health promoters to both understand and apply an epigenetic approach to effective obesity prevention and intervention programming.

2.1.5 Biological processes in genetics, epigenetics, and gene activity

Epigenetics is the study of potentially heritable changes in gene expression (activity) and/or gene inactivity (silence) that do not involve changes to the underlying DNA sequence (Jaenisch & Bird, 2003). Epigenetic mechanisms involve phenotype changes without genotype changes and affect how cells "read" their genes. Epigenetic

changes are influenced by several factors including biological age, environment, lifestyle, and disease states. Environmental conditions and factors can control a promoter to express or silence a gene (Campion et al., 2009; Jaenisch & Bird, 2003). Three epigenetic mechanisms that can modify gene expression during the normal development of an organism and can result in diseases such as obesity, diabetes, and cancers, are most commonly known as DNA methylation, histone acetylation or de-acetylation (histone modification), and non-coding RNA (ncRNA)/small RNA (snRNA) (Campion et al., 2009; Holliday, 2006).

Epigenetic mechanism: DNA methylation

DNA methylation can act as an epigenetic marker accounting, mainly, for gene inactivation or gene silencing. Riggs (1975) were the first to propose the association between DNA methylation and gene inactivation. The distinct enzyme called methyl-transferase was identified as responsible for DNA methylation.

Following Bird (1978) and Bird and Southern's (1978) discovery that DNA methylation causes gene silencing, much attention has been focused on DNA methylation patterns and the mechanism has become a new focus for understanding gene regulation and gene expression. DNA methylation occurs when enzymes called DNA methyl-transferase add methyl (and acetyl – or small chemical groups) to the DNA, at the region of the DNA called CpG sites or CG pairs. The presence of certain amounts of these chemical groups (methyl or acetyl) at that location can turn a gene off; their removal turns the gene on, again. DNA methylation also plays an important role in

genomic integrity, ensuring the proper function of all the genetic elements in an organism (Bestor, 1998; Hedges & Deininger, 2007).

Epigenetic mechanism: Histone acetylation

Histones are proteins that bind themselves to DNA molecules or to their nucleus, "acting as spools around which DNA winds" itself (Wikipedia, 2017a, para. 1). For every chromatin structure (i.e., "a complex of macromolecules found in cells, consisting of DNA, protein, and RNA") (Wikipedia, 2017b, para. 1), there are 146 DNA wraps around the 2 units of H1 (one of the five histone families), a single unit of H3, and an H4 protein (Wikipedia, 2017a).

Histone acetylation occurs when enzymes called "histone acetyltransferase" facilitate the process of transferring one acetyl functional group from one molecule to another. Allfrey and Mirsky (1964) speculated that histone acetylation made the gene more accessible to transcription and led to gene expression. They also reported that the histone acetylation process causes the chromatin to become "active." Histone acetylation is often associated with repression of gene activity (Yan & Boyd, 2006).

Histones can be modified by various processes besides acetylation: methylation, sumoylation, ADP ribosylation, and phosphorylation. The most common histone modifications are histone acetylation and DNA methylation of lysine in the H3 and H4 proteins (Suganuma & Workman, 2008).

Epigenetic mechanism: Non-coding RNA or small RNA

Histone modifications or histone remodeling can be achieved not only by histone proteins but also by small or non-coding RNAs (Costa, 2008). Non-coding RNA (ncRNA) is a "functional RNA molecule that is transcribed from DNA but not translated into proteins" (Whatisepigenetics.com, n.d., para. 1). Increasing evidence indicates that non-coding RNAs are capable of recruiting and binding regulatory complexes within the non-coding DNA sequence (Chu, Qu, Zhong, Artandi, & Chang, 2011). However, how the non-coding RNA mechanism can be transmitted to subsequent generations through cell divisions remains unclear. Although their role in epigenetic transmission is puzzling, many studies have revealed that non-coding RNAs play an important role in affecting and modifying the histone structure and functional state of chromatin (Costa, 2008; Chu et al., 2011).

2.2 Brief history of epigenetics

2.2.1 Evolution of epigenetics

Epigenetics is the study of inheritable changes that alter gene expression without changes in the underling DNA sequence (Holliday, 1994; Riggs and Porter, 1996). Current definitions of epigenetics are limited to our understanding of DNA. Despite the fact that each cell type contains identical DNA information, gene expression patterns are essentially very different among different types of cells. Therefore, Riggs, Martienssen, and Russo (1996) have defined epigenetics as "The study of mitotically and/or

meiotically heritable changes in gene function that cannot be explained by changes in DNA sequence," (p. 1).

Developmental biology and genetics scientists Conrad H. Waddington and Ernst Hadom were considered the pioneers of epigenetics. In 1942, Waddington described the influence of the genetic process on development. Waddington was the first scientist to connect the concept of gene plasticity to evolution and adaption processes through epigenetic regulation. In 1952, Waddington observed that environmental stress can cause phenotypic change in *Drosophila* fruit flies. He demonstrated that embryo fruit flies show different phenotypes by simply changing the environmental temperature or a chemical stimulus in the environment (Waddington, 1952). Furthermore, he showed how the developmental plasticity of individual genes, could change and adapt to environmental conditions and influences, leading to changes without DNA mutations (Noble, 2015). Waddington (1952) used the term "epigenetics" to categorize all of an organism's events, from fertilized zygote to maturity, as well as gene regulation including genetic materials and shaping of the final product.

From the time Waddington proposed his definition of epigenetics, there has been much debate among biologists and embryologists about the nature and developmental processes of cells and organisms. More recently, for instance, Felsenfeld (2014) proposed that each cell exhibits preformed elements ("preformationism"), in other words they enlarge during development, and that "epigenetics" which involves environmental and developmental processes focuses on the importance of developmental processes associated with the nucleus and cytoplasm. Although the definition of epigenetics has

been changing, it is crucial to coin the original problem as: "How can a single fertilized egg give rise to a complex organism with cells of varied phenotypes?" (Felsenfeld, 2014, p. 2). Evidence from *Drosophila* genetics suggests that phenotypic changes can occur without changes in genes or DNA sequence, which conflicts with the "central dogma" system (DNA-RNA-Proteins) known as the primary genetic information carrier (Koonin, 2012; U.S. National Library of Medicine, 2017). Since the conflict was notices, the definition of epigenetics has centered on changes in gene expression without changes in the underlying DNA sequence within a cell's nucleus.

In the last decade, many studies have focused on uncovering the epigenetic mechanisms related to phenotypic changes. DNA methylation is one of the most well-known and well characterized epigenetic mechanisms. Griffith and Mahler (1969), for example, found that DNA methylation has caused epigenetic changes associated with long-term memory function, cancers, mental retardation/disorders, immune disorders, and psychological and pediatric disorders.

Earlier epigenetic theories proposed that epigenetic changes can be erased during embryonic development and that previous epigenome tags will be wiped out and re-developed, afresh. However, several studies — from animal models to human studies — suggest that epigenetic tags/markers established during the course of a life-span can pass onto subsequent generations (Morgan, Sutherland, Martin, & Whitelaw, 1999; Probst, Dunleavy, & Almouzni, 2009; Rakyan & Whitelaw, 2003; Roseboom, de Rooij, & Painter, 2006; Tobi et al., 2014).

2.2.2 Empirical evidence

Epigenetics is the study of gene and environment interactions, linking DNA methylation, histone acetylation, and non-coding RNA or small RNA to external environmental cues. In other words, epigenetics brings genes and the environment together.

A classic example of epigenetic evidence of gene and environment interactions goes back to the brutally cold winter of 1944-45 (November to Spring) known as the Dutch Hunger Winter in the Netherlands (Stein et al., 1975). Following a railway strike, German blockades led to a catastrophic drop in the availability of food, nation-wide. The famine affected people from all social classes. Adults, including pregnant mill, received about five hundred calorie per day, which was less than one-third the daily caloric intake need for adults. Following the tragic winter famine, however, the Dutch enjoyed growing prosperity. Nevertheless, the winter of 1944-45 left significant marks on their health and wellbeing.

This well-documented catastrophic famine and social stressor became the focus of many on-going epidemiologic studies. Researchers have compared exposed/unexposed cohorts of survivors, through infancy, childhood, adulthood, and their subsequent generations. The first epidemiologic studies focused on neurodevelopment, then were later extended to examine a broad range of health outcomes, including obesity, cardiovascular diseases, reproductive performance, as well as breast and ovarian cancer (Hoek, Brown, & Susser, 1998; Susser, Hoek, & Brown, 1998). Furthermore, in the mid-1980s, the original investigators extended their study to

intergeneration linkages — early prenatal famine exposure and its effects on subsequent offspring and their health (Susser et al., 1998). More recently, researchers have also examined the effects of: under-nutrition (Desai, Gayle, Babu, & Ross, 2005, Jones & Friedman, 1982; Oliver, 2012; Rumball, Harding, Oliver, & Bloomfield, 2008), over-nutrition such as a high fat and calorie-dense diet) (Hawkes, 2006; Howie, Sloboda, Kamal, & Vickers, 2009), and environmental toxins (Welshons, Nagel, & vom Saal, 2006), as well as their effects on subsequent rates of adult obesity and cardiovascular risks (Schulz, 2010). Accelerated aging associated with cognitive complications had also been examined in the gestations exposed to the Dutch Hunger Winter (de Rooij, Wouters, Yonker, Painter, & Roseboom, 2010).

Follow-ups to the Dutch Hunger Winter study have discovered that the early intrauterine environment(s) had long-term consequences for adult health later in life. Babies born to women exposed to the famine during *early gestation* weighed less than the babies born to women exposed during mid or late gestation periods. Although babies exposed to the famine during the mid and late gestation were born with normal weight, they faced more frequent reduced renal function than those exposed during early gestation (Roseboom et al., 2006).

The environment interactions with developing embryos appear to not affect birth weight, exclusively. At ages 56-59, people who experienced early gestation exposure to famine were found to continue having the impairment (obesity and related diseases) (Lumey et al., 2009; Roseboom et al., 2001; Roseboom et al., 2006).

These findings have been rather consistent and made significant contributions to the growing field of Development Origins of Health and Disease (DOHaD) (Schulz, 2010). Because designing and conducting a similar study would be unethical, the Dutch Hunger Winter follow-up studies have provided a crucial insight regarding: 1) how an adverse fetal environment influences epigenetic fitness; 2) how epigenetic changes alter metabolic/adipose gene regulation and function and influence the health and diseases of adults later in life, and 3) evidence that a stressful early environment can affect not only current generations but also their offspring (their children and their children's children).

Roseboom et al. (2006) found that when the early gestation exposure babies grew up, they had higher rates of obesity, altered lipid profiles, and cardiovascular diseases than those exposed during the mid and late gestation trimesters (or those born before and after the war). In addition to these studies, Jones and Friedman (1982) used a rat animal model to mimic undernourishment during pregnancy. The lack of nourishment led to the development of obesity as well as adipocyte abnormalities in their offspring (Jones & Friedman, 1982). Similarly, Bispham et al. (2003) used a sheep model to manipulate nutritional consequences associated with maternal plasma leptin and cortisol, or maternal endocrine adaptations throughout pregnancy, and found that programming of fetal adipose tissue development in the offspring occurred.

Stein et al. (1975) provided additional insights into the gene and environment interactions that affect epigenetic changes associated with prenatal stress and subsequent adult obesity as well as obesity-related metabolic syndromes and cardiovascular health. These authors also documented that the children conceived during that Dutch Hunger

Winter, especially those whose mothers consumed less than the minimum required calories/nutrition during early pregnancy, suffered significant consequences later in life associated with metabolism and cardiovascular health (Stein et al., 1975).

Such comparisons between early and mid or late intrauterine stages of exposure and consequences for the fetus in later life, also led to the notion of a "critical window" in an organism's development — both human and animal. Additionally, the epigenetic association of adult obesity with intrauterine environmental stress and calorie restriction has been replicated in rodent and sheep animal models (Calkins & Devaskar, 2011; Jirtle & Skinner, 2007; Lillycrop & Burdge, 2011).

Recently, a group of researchers from the U.S. and The Netherland (Heijmans et al., 2008) followed the Dutch Hunger Winter's babies, who are now around the age of 60. The researchers collected these now-adults' blood samples and compared 1.2 million CpG DNA methylation sites with their biological same-sex siblings not exposed to the Hunger Winter. They found those exposed to the famine had different gene regulation despite the fact that both groups had a similar genetic inheritance and family history or background. They also found that the gene activity setting was differentially regulated for those exposed to the famine (compared to their siblings without exposure to the famine). The babies conceived during the famine, even though born with an average birth weight, exhibited altered epigenetic regulatory systems of growth associated with metabolic and developmental groups of genes. This phenomenon may also explain why they have a significantly higher risk for metabolic diseases and obesity in later life (Heijmans et al., 2008).

This study demonstrated that environmental factors during the critical stages of life development can make a lasting impression on the gene regulatory system that determines which genes will "turn on" or "turn off." Such findings provide a tremendous opportunity for epidemiologists, health educators, and health professionals. "Looking at the human genome, we see systematic changes in gene regulation during early human development in response to the environment. The epigenetic revolution has given us the tools to investigate these changes and look at the impact for later life," — claims L.H. Lumey (Columbia University's Mailman School of Public Health, 2014, para. 7), the senior author of the epidemiology studies at Columbia University's Mailman School of Public Health. Studies reported by Lumey and others revealed that early human development is especially sensitive to environmental factors and can cause systematic changes in gene regulation in response to the environment, some of which will only manifest themselves years later (Dolinoy, Weidman, & Jirtle 2007; Lumey et al., 2011; Lumey, Stein, & Susser, 2011). Hunger and harsh environments can create vulnerability to obesity in current and future children through poor nutrition and starvation experienced by the mother.

Another practical example of epigenetic influence on human health is related to toxins such as bisphenol A (BPA), a chemical present in polycarbonate plastic, associated with higher body weight and cancers (breast and prostate cancers, in particular). Using a yellow agouti (A^{vy}) mouse model, Dolinoy, Huang, and Jirtle (2007) demonstrated that pregnant mice exposed to BPA had a decreased CpG (cytosine-guanine dinucleotide) DNA methylation at the A^{vy} locus and an altered epigenetic pattern

during the early stem cell development. Consequently, their offspring had higher body weight and an increased risk of breast and prostate cancer. Additionally, the BPA exposure of the mothers decreased CpG methylation in the Agouti gene (A^{vy}), which contains DNA coding for visible coat color, and consequently shifted the coat color of the mouse offspring from brown to yellow.

Interestingly, researchers have also learned that the gene-environment interactions influencing DNA methylation and causing epigenetic changes associated with gene expression are reversible and the reversal can be passed on to subsequent generations. Dolinoy, Huang, and Jirtle (2007), for instance, reported that diet alteration can offset the effect of BPA exposure. They fed the pregnant mice exposed to BPA a dietary supplement containing a plant phytoestrogen rich with genistein (found in soy products). Their result was stunning — the offspring of the mice fed with this diet shifted their coat color back to brown (in other words, the methyl-enhancing diet counteracted the effects of the BPA exposure). In other words, Dolinoy, Huang, and Jirtle (2007) demonstrated that environmental and nutritional alterations can change DNA methylation, one of epigenetics' main mechanisms. Put simply, DNA methylation can be altered and reversed. Decreasing DNA methylation (exposure to BPA) shifted the coat color toward yellow, and increasing DNA methylation (with a methyl-rich diet) restored the coat color back to brown (Dolinoy, Huang, & Jirtle, 2007).

2.3 Factors affecting epigenetics

The field of epigenetics has grown quickly during the last, post-genome decade (Heard et al., 2010). From animal models to human studies, scientists have found many internal and external factors including social, psychological, environmental, and lifestyle factors that can directly interact with the genome and the epigenome, affecting gene function through epigenetic change mechanisms. Such changes may impact the epigenome throughout the course of an organism's life, and they can also be passed on to subsequent generations. Below, I will examine some of the most common factors believed to lead to important epigenetic changes.

2.3.1 Physical activity

The benefits of physical activity or exercise have been known for a long time. Scientists have long established that physical activity can lower risk of cardiovascular disease, obesity, and many weight related health problems (U.S. Department of Health and Human Services, 2008). Recent epigenetic studies have shown that six months of physical activity can increase DNA methylation of specific genes related to the risk of chronic diseases. Studies have also linked exercise with alteration in proinflammatory cytokines' gene methylation. DNA methylation in such cases will silence the proinflammatory gene, therefore reducing the risk of cancer development, among other illnesses (Zhang et al., 2011).

Conversely, *sedentary* lifestyles have been blamed for overweight and obesity. Rönn and colleagues (2013) conducted a six-month exercise intervention (one-hour

spinning session and one-hour aerobics per week) for *sedentary* men. They found DNA methylation changes occurred in T2D and obesity-related genes in their adipose tissue. DNA methylation turned off and silenced the obesity related genes' functions. Therefore, endurance exercise impacted fat storage and metabolism rates, in these samples, *regardless* of family history of T2D or obesity (Rönn et al., 2013).

Thune, Brenn, Lund, and Gaard (1997) followed a cohort of 25,624 women for 13.7 years and examined the link between physical activity and risk of breast cancer. They found a lower risk of breast cancer associated with greater leisure time spent on physical activity (Thune et al., 1997). Furthermore, Barres et al. (2012) also discovered epigenetic changes resulting from exercise lowered not only the risk for disease but also impacted performance. They compared skeletal muscle before and after an acute bout of exercise and found that study participants post-exercise had fewer methyl groups in energy metabolism (genes such as PGC-1a, PPAR-õ, PDK4) than pre-exercise. Barres and colleagues (2012) found that just a single exercise session was associated with expression of genes related to energy breakdown, while energy metabolism genes remained methylated and silent. They also found that greater intensity of skeletal muscle workouts generated a higher amount of DNA methylation (Barres et al., 2012). However, exercise-induced epigenetic changes did not appear permanent since they did not alter the DNA sequence. When exercise discontinued, epigenetic modifications reverted back to their original state (Barres et al., 2012).

Zhang et al. (2011) also documented evidence that epigenetic mechanisms may be involved and affected by physical activity. For example, post physical activity, study

participants had increased DNA methylation of long interspersed nucleotide element (LINE)-1 in bold peripheral lymphocytes (LINE-1 element is a highly repeated sequence in human genomes and is associated with inflammatory responses and chromosome stability). Baccarelli, Rienstra, and Benjamin (2010) found that active older adults with high LINE-1 methylation in peripheral blood lymphocytes had a lower incidence of obesity-related heart disease/stroke or mortality The study further showed that physical activity leads to H3K36 gene acetylation in human muscle (Baccarelli et al., 2010). Furthermore, Radom et al. (2012) documented alteration of miRNA profiles in circulating neutrophils in a study with brief bouts of physical activity.

Zhang et al. (2011) compared a group of people spending 26 to 30 minutes a day exercising, to those spending less than 10 minutes a day. They found the group exercising longer had more DNA methylation than the other group. Zhang et al. (2011) also indicated that both the amount of time and the level of daily exercise mattered for the average person to develop positive epigenetic changes.

2.3.2 Age, lifestyle factors and parental obesity

In human studies, there is evidence that parental lifestyle factors affect the offspring's epigenome. Soubry et al. (2015) conducted the Newborn Epigenetics Study (NEST) by examining 79 newborns' umbilical cord blood samples, collected between November 2006 and July 2015. Multiple regression models were used to determine the association between parental preconception obesity (with BMI greater than 30 kg/m^2) and the offspring's DNA methylation pattern. They found hypomethylation in the

Insulin-like Growth Factor 2 (IGF2) gene, and different methylation regions (DMRs) were associated with parental obesity ($\beta = -5.28$, $p = 0.003$). Even after adjusting for maternal and newborn characteristics such as both parents' BMI, maternal age or smoking status, the newborn's birth weight and gender, they found a persistent inverse pattern of parental obesity associated with Insulin Growth Like factor 2 (IGF 2) hypomethylation in newborns, increasing their risk of chronic diseases later in life (Soubry et al., 2015).

2.3.3 Tobacco use

Epigenetic alternations associated with prenatal smoking, which can lead to tobacco-related illnesses, have also been discussed by several authors (Breton et al., 2009; Suter, Anders, & Aagaard, 2012). For example, several cohorts of adults and young people, both smokers and nonsmokers, have been compared using the high throughput epigenetic genome-wide studies and researchers have detected consistent alterations associated with DNA methylation in several genes *F2RL3 AHRR,GPR15* (Gao, Jia, Zhang, Breitling, & Brenner, 2015). Tobacco smoking emerged as a strong predictor of negative health outcomes in these studies. Genome-wide approach studies have found that tobacco smoking during pregnancy is associated with epigenetic changes at the global as well as gene-specific levels and that these changes persist well into childhood and adolescence of the offspring (Breton et al., 2009; Seisenberger, Peat, & Reik, 2013).

Passive smoking also is a risk factor for acute, chronic, and lifelong morbidity. There is ample evidence linking passive smoking to reduced birth weight (England et al., 2001; Wang et al., 2002; Windham, Eaton, & Hopkins, 1999); smaller head circumference at birth (Robinson, Moore, Owens, & McMillen, 2000); increased sudden infant death syndrome (SIDS) (Dybing & Sanner,1999; Godfrey & Barker, 2000); infection (Kriz, Bobak, & Kriz, 2000); reduced lung function and allergic sensitization (Strachan & Cook, 1998); middle ear diseases (Strachan & Cook, 1998); wheezing (Strachan & Cook, 1998); adult asthma, chronic obstructive pulmonary diseases (COPD), neurodevelopmental and behavioral problems (Brennan, Grekin, Mortensen, & Mednick, 2002; Wakschlag, Pickett, Cook Jr., Benowitz, & Leventhal, 2002); and childhood cancers (including all neoplasms) (Boffetta, Trédaniel, & Greco, 2000; Filippini et al., 2002). Prenatal smoking has lifetime consequences for the offspring of smokers, due to passive smoking influences on placental and fetal development (Boffetta et al., 2000).

In the Avon Longitudinal Study of Parents and Children (ALSPAC), conducted by Carslake, Pinger, Romundstad, and Smith (2016), early onset of parental smoking (as early as ages 11-14 years) was found to be associated with epigenetic modifications in the germ line, affecting intergeneration and offspring males' adiposity and elevated BMI, fat mass and waist circumference. Using the Nord-Trondelag Health (HUNT) study, researchers found that parental smoking at age 11 was not strongly associated with the BMI of sons aged 12-19. However, among daughters, researchers found an association between early-age parental smoking and offspring's BMI, fat mass and waist

circumference for the age range from 12.1-76 years (mean age of 29.1 years) of the offspring. The pattern was consistent for the daughters examined in a sample of more than 45,000 offspring (Carslake et al., 2016).

Another example: Northstone, Golding, Smith, Miller, and Pembrey (2014) analyzed data collected from 9,000 fathers in the ALSPAC, on smoking behavior ,and found a positive association between parental tobacco smoking and son's BMI, waist circumference and fat mass (son's ages ranged between 7 and 17 years) (Northstone et al., 2014).

2.3.4 Family history of obesity

Obesity is linked directly to T2D, cardiovascular diseases, and certain forms of cancer. Adipose tissue plays a central role in the development of obesity-related health issues and is controlled by the endocrine system, affecting metabolic pathways including glucose homeostasis (i.e., the body's self-balancing of insulin and glucagon to maintain blood glucose) (Rönn et al., 2013). Epigenetic mechanisms, including DNA methylation and histone modification, can affect the development of obesity, independent of a family history of obesity. Studies have shown that environmental, lifestyle, behavioral, psychological factors, pathological stimuli, and age have the potential to modulate epigenetic reprogrammming patterns of gene expression at the early developmental stages, increasing the risk of obesity in later life (Godfrey & Barker, 2000; Waterland & Jirtle, 2004). Individuals with family history of either one or both parents being obese might have a higher risk of developing obesity. However, altering environmental and

lifestyle factors, including diet and exercise, has the potential to change epigenetic profiles (Qi & Cho, 2008; Reddon et al., 2016).

2.4 Implementation of epigenetics in health education and health promotion

Epigenetic mechanisms alter gene expression and can pass these alterations to subsequent generations (Dunn & Bale, 2011). Epigenetic changes occur at the phenotypical level without changing the underlying DNA, which simply means that organisms might have various phenotypes (physical appearances) with an identical genotype (DNA sequence). Epigenetic changes in gene expression (active or inactive) and gene functions (expression or silence) happen not only in association with disease states but also during the regular development process. For instance, there are more than two hundred different cell types within the human body. Each cell type has identical DNA sequences and genetic information, but each cell type has very different gene expressions and gene functions depending on its foundations. Not all genes are expressed at the same time or in the same way. Only necessary and functional genes are being transcribed from DNA to RNA, translated from RNA, and then expressed as functional proteins (National Institute of Health, 2017a).

DNA sequences don't accomplish anything without being transcribed/translated into functional proteins. The information stored in DNA needs to be read during a particular biological process to initiate gene transcription/translation in order for the gene to become functional, and for the process to result in the gene's product(s) – the proteins. Of all the DNA within the cell or organism, only a small fraction is active at

any given time. The majority of the human genome is, in fact, inactive (National Institute of Health, 2017a).

Epigenetic changes happen as a response to environmental and other lifestyle factors, as opposed to genetic changes, which are due to inheritance or mutations. Given these characteristics, it follows that altering environmental and lifestyle factors can be easier than modifying or changing genetic traits.

Gene-environment interaction studies in both animal and human models have helped understand how individuals with identical genotypes have different responses to various environmental and lifestyle factors and how these responses change over the course of a lifetime (de Rooij et al., 2010; Schulz, 2010). Such studies linking genes and the environment have highlighted the significant contribution of genetic and environmental or epigenetic variability to obesity and other human diseases. Therefore, it is important for health educators and public health professionals to apply what is currently known about epigenetic mechanisms in intervention and health promotion programs. Health promoters/educators can, for instance, emphasize nutrition and environmental factors as these factors influence fetal, adult and transgenerational epigenetic gene regulation, resulting in numerous phenotypic consequences.

In light of new knowledge and development in overweight/obesity (and its associated health complications), health educators need to broaden their knowledge and adapt epigenetics/genetics approaches into their practice. To this end, the following suggestions are in order:

1) Health educators should become familiar with the scientific literature on epigenetics and understand how epigenetics "works."

The familiarity includes learning about gene, environment and lifestyle interactions, as well as gene expression (as demonstrated in animal and human studies). In other words, health educators should learn about epigenetic mechanisms and how they respond to environmental and lifestyle factors. Further, based on the findings of my study (see Chapter 3), it is crucial to investigate further what factors are associated with epigenetic changes, and when is the most effective epigenetic window for introducing interventions in order to prevent future generations from becoming obese. It is also important to explore and understand the role that nutrition, physical activity, and other lifestyle factors play in causing overweight and obesity through epigenetic mechanisms. For decades, health educators have promoted healthy lifestyles, physical activity, smoking cessation, and exercise, but they have done so without fully grasping the biological mechanisms/links supporting their efforts. A better understanding of *how* tobacco smoking, for instance, can shape epigenetics and affect the offspring of smokers may provide a stronger rationale for prevention efforts than merely emphasizing the immediate benefits of smoking cessation for the smoker, alone.

2) Health education training programs should enrich their degree and professional training by adding an epigenetics perspective.

Currently, little emphasis is placed, in Health Education curricula nationwide, on epigenetic mechanisms. For example, there is a lack of training in genetics, epigenetics,

and nutrition for students in current health education and healthcare undergraduate, graduate, and professional degree programs (Ettienne-Gittens et al., 2011; Thunders, 2015). If future health educators lack the necessary knowledge of nutrition, physical activity, genetics, epigenetics, and genomics, their ability to apply systematic and science-based approaches to tackling the overweight and obesity issue will be significantly limited.

3) Health educators should continue to fight for adding health education into K-12 grades in schools, with epigenetics as part of the curriculum.

Despite the alarming obesity rates — 1/3 of U.S. adults are clinically obese, and almost 1/6 of U.S. children aged 2-19 are currently obese (National Center for Health Statistics, 2017) — formal health education in schools, K-12 grades, is lacking. The National Center for Education Statistics (2006) showed that only 50% of school children in K-8 grades, 40% of junior high school students (grades 9-10), and 20% of high school juniors and seniors (grades 11-12) were offered or required to take health education classes in 2005. In 2012, Texas schools abolished a half-credit-hour health education course, which had been a requirement for high school graduation (Texas Education Agency, 2012). Nutrition courses must also be part of student health education in schools and the topic needs to be discussed continually after that.

Moreover, while the U.S. Department of Health and Human Services (2008) recommends at least 60 minutes of physical activity daily for children and youths aged between 6 and 17, there is no mandate for schools to offer physical education. A study

conducted by the National Center for Education Statistics (2006) found that only 17-22% of public schools in the U.S. offered daily physical education classes, and that 22% of elementary schools scheduled physical education once a week for K-8 grades. Furthermore, the Centers for Disease Control and Prevention (CDC) (2017) reported that only 29.8% of high school students attended physical education daily, and only 21.6% of 6 to 19-year-old in the U.S. participated in sixty or more minutes of moderate-to-vigorous physical activity five times per week.

With the lack of health education and daily physical activity among K-12 students, the consequences of low physical activity and poor diet choice will extend into their adulthood and increase their chance to develop overweight and obesity. Studies have shown that for overweight/obese children, at least two-thirds of them will stay overweight/obese as an adult (CDC, 2013).

4) Health educators should continue to emphasize prevention of overweight/obesity.

Tremendous efforts have been geared to find treatments for overweight/obesity-induced diseases and to identify the gene(s) that can control overweight and obesity. These efforts are expensive and yet have not generated expected outcomes. More cost-effective measures to address the public health issue of overweight and obesity would be to offer more prevention programs rather than treatments. Health educators can and should play an increasingly important role in developing and executing such prevention programs (HealthyPeople.gov, n.d.; Roberto et al., 2015).

Based on the 2012 National Health Interview Survey (NHIS) data (National Center for Health Statistics, 2017), more than half of U.S. adults indicated they were physically unable to do strength training and vigorous physical activity although strength training and vigorous physical activity are among the most effective means for weight control (da Mota, Orsatti, da Costa, & Júnior, 2010). Therefore, slow and steady weight loss interventions might be the first step to help those who are overweight or obese, as studies have demonstrated that a reduction as small as 5% in weight can reduce, eliminate or prevent coronary heart disease, T2D, hyperlipidemia, hypertension, cardiorespiratory failure, stroke risk, and other chronic diseases (Pasanisi, Contaldo, de Simone, & Mancini 2001). To promote offering more prevention programs, there is an urgent need to increase the priority and funding for promoting a healthy lifestyle and environmental changes for children, youth, college students, and adults (Benjamin, 2010; HealthyPeople.gov, n.d.; the Trust for America's Health and the Robert Wood Johnson Foundation, 2017).

5) Health educators should focus on longer-term commitments and fundamental solutions.

Weight gain and obesity do not happen overnight, neither does weight loss. Further, overweight and obesity are widespread and attributable to many factors. Hence, it is impossible to have a "quick fix" to this issue, and any "quick fix" is unlikely to solve the overweight and obesity problem fundamentally. Unfortunately, many of existing studies, research funding programs, and health education and intervention

programs lack a longer-term focus or commitment (Flynn et al., 2006; Miller et al., 1997).

In summary, this chapter's goal was to help inform future health educators and public health researchers of the importance of becoming aware of current developments in epigenetics and related fields, and of collaborating across multiple disciplines including genetics, epigenetics, the social and the environmental sciences. Acknowledging and responding to multidisciplinary research needs is critical to innovative and effective health education and promotion. Incorporating epigenetic mechanisms and recognizing disparities in addressing the overweight and obesity issue will provide a unique opportunity to advance health education and intervention, to promote the culture of health for life, and to prevent (and treat) the problems of overweight, obesity, and their complications.

3. ASSESSING SOCIO-DEMOGRAPHIC, ENVIRONMENTAL, AND LIFESTYLE FACTORS ASSOCIATED WITH OVERWEIGHT AND OBESITY AMONG ADULTS IN THE U.S.

3.1 Background and objectives

For the last few decades, body mass index (BMI) ratios have increased exponentially in the U.S. (National Center for Health Statistics, 2017). While the genetic trait of height has stabilized in the U.S. population (in the last 150 years or more) body weight has continued to increase due to overweight and obesity (Cole, 2003). Increasing BMI ratios are mainly due to body fat deposits, which can lead to many chronic diseases (Reilly et al., 2003). These increasing BMI ratios, alongside increases in overweight and obesity have become a nationwide public health concern and an economic burden, affecting the nation's long-term prosperity and security (Finkelstein et al., 2009; Mokdad et al., 2001; Williams, 2016).

A considerable amount of research has been undertaken to unveil the causes of overweight and obesity, including genetic-based research. Extensive literature (reviewed in Chapter 2) suggests, however, that genetics alone cannot explain the current widespread overweight and obesity problem in the U.S. and that epigenetic, socio-demographic, lifestyle, and environmental factors are the major culprits in the overweight and obesity epidemic. A recent study by Temelkova-Kurktschiev and Stefanov (2012), for instance, reveals that most genes known so far have only a modest effect on obesity and related morbidity risk. They found that obesity and T2D have low

probabilities of developing outside a promoting environment, and that unhealthy lifestyles, especially physical inactivity and food overconsumption, are the main reasons behind obesity and T2D (Temelkova-Kurktschiev & Stefanov, 2012). A recent report by the Harvard School of Public Health indicates that genes or heredity are not destiny and, instead, points to the importance of gene-environment interactions in the severe and widespread overweight and obesity issue (Harvard School of Public Health, 2017). These studies/reports suggest there is a compelling need to examine socio-demographic, lifestyle, and environmental determinants of overweight and obesity, aside from their genetic causes.

Linking socio-demographic, lifestyle, and environmental factors to overweight and obesity not only enhances the understanding of non-genetic reasons for the overweight and obesity epidemic, but also offers useful implications for developing and implementing future health education and intervention programs. If health educators and public health professionals wish to see lower BMIs and solve obesity-related health problems, they would do best to focus on the changeable factors that affect the everyday life of individuals. One's lifestyle and environmental factors are relatively easy to change compared to one's genetic makeup.

Although a variety of socio-demographic, lifestyle, and environmental factors are considered determining factors for overweight and obesity, few studies have linked overweight/obesity to multiple factors, simultaneously, and in a systematic manner (Hill & Peters, 1998; Silventoinen, Rokholm, Kaprio, & Sørensen, 2010). Many previous weight-loss studies, instead, have focused on either a single or a small set of variables

and assumed the linear and isolated effect of a specific factor on overweight and obesity. For example, studies have linked overweight/obesity and related diseases to age, ethnicity, and socio-economic status (Jeffery et al., 1991), fast food consumption (Karter et al., 1996), breakfast skipping (Reutrakul et al., 2014), fruit and vegetable consumption (Rautiainen et al., 2015), and sleep (Reutrakul & van Cauter, 2014). In addition, studies have examined sedentary activities such as addiction to TV/computer/video games and have found positive associations with overweight and obesity (Tomlin et al., 2014). These studies are significantly limited because they fail to portray the complex relationships between overweight/obesity and a wide range of factors interacting simultaneously. As such, these studies' findings can only guide piecemeal approaches to address the overweight and obesity issue, and these approaches have, so far, proven to be limited or ineffective (Blackstone, 2016; Chan & Woo, 2010; Flynn et al., 2006; Roberto et al., 2015; Wang et al., 2013).

To advance knowledge of the complex association between overweight/obesity and lifestyle or environmental factors, and to provide guidance for more comprehensive/effective health education and intervention programs, it is imperative to take into account the joint nonlinear effects of a wide spectrum of relevant factors on overweight and obesity. With this in mind, the objectives of this study are to:

1) Identify socio-demographic, environmental, and lifestyle factors (SDELFs) that are associated with overweight and obesity, among a nationally representative sample of adults in the U.S.; and

2) Assess the nonlinear statistical association among socio-demographic, environmental, and lifestyle factors and overweight and obesity risk among the U.S. adult population.

An array of SDELFs is considered, including different levels of physical activity (sedentary, moderate, vigorous, and strength conditioning), smoking, alcohol consumption, hours of sleep, marital status, regions of residency, age, and race/ethnicity. Using BMI, body weight status is classified into: underweight, normal weight, overweight, and obesity. By comparing the risk to be overweight or obese relative to normal weight, this study helps better understand which factors have a positive or negative effect on the BMI of U.S. adults in a more holistic manner. Such understanding can provide useful guidance for more effective health education and intervention programs.

3.2 Methods

3.2.1 Data source

In this study we drew data from the 2012 National Health Interview Survey (NHIS). The NHIS was conducted by the National Center for Health Statistics (2017), under the Centers for Disease Control and Prevention (CDC). The NHIS data, collected yearly since 1957, represent the largest in-person household health survey of U.S. civilian health status, medical service accessibility, and other health related behaviors. The U.S. Census has been the data collection agent for the NHIS for over 50 years. The

NHIS data are made publically available, with a lag time of approximately two years, at the website maintained by the CDC (National Center for Health Statistics, 2017).

3.2.2 Survey sample and variable selection

The NHIS data were gathered by cross-sectional household interview surveys with non-institutionalized, randomly selected civilians in the U.S. The sampling approach ensured the adequate inclusion of Black, Hispanic, and Asian adults and those over 65 years old, excluding active-duty armed forces personnel and those from long-term care facilities and correctional facilities. The sample consisted of 428 primary sampling units (PSUs) covering all the 50 states and the District of Columbia. A PSU is a county or a metropolitan area. Detailed information associated with the NHIS data collection procedures is available from the National Center for Health Statistics (2017).

The NHIS 2012 sample consisted of 34, 525 persons who were at least 18 years old. Most of the survey participants completed the questions on their own, unless an individual was unable to do so physically or mentally (only 468 of 34,525 adults). There is no compensation/incentive provided for the participants in the NHIS. Additional information about the survey responses can be found in NHIS 2012 Appendix I (National Center for Health Statistics, 2017).

From the NHIS data, I selected BMI and multiple socio-demographic, environmental, and lifestyle factors including age, sex, race/ethnicity, region, smoking, alcohol consumption, physical activity (three levels), marital status, and hours of sleep. The 2012 NHIS dataset contained more than 800 variables, from which I chose 13

variables (one as the dependent variable and 12 as independent variables) with 36 sub-variables.

The selection of these variables was guided, primarily, by empirical evidence described in the scientific literature (described in Chapter 2), which suggests these variables are likely to be associated with overweight or obesity. Few studies, however, have assessed all these variables in tandem. These variables also represent a wide spectrum of socio-demographic, lifestyle, and environmental factors that are of interest to health educators and professionals. Additionally, there were few missing data (non-responses) for these variables in the 2012 NIHS dataset, making them good candidates for regression analysis.

The missing data along with applicable non-responses were excluded from this study. Due to the nature of the in-house survey, missing data were not very common for the variables selected. According to the NHIS 2012 data manual, codes "7, 97, 977, etc." mean "refusal," code of "8" indicates "not ascertained," and code "9" indicates "unknown." These "refusal," "not ascertained," and "unknown" responses along with those "unable to do it" and the missing data were combined and excluded from this statistical analysis. The number of non-responses and missing observations varied with variables and, overall, was relatively small. The highest number of missing/non-applicable responses was reported for the variable "drinking," with 732 missing observations.

3.2.3 Coding of selected variables and their frequencies

The original data from the 2012 NHIS were recoded for statistical analysis. The codes of the selected variables and their frequency distributions/mean are shown in Table 1. BMI was classified into four categories: underweight (BMI < 18.5 kg/m^2), normal weight (18.5 kg/m^2 ≤ BMI < 24.9 kg/m^2), overweight (25 kg/m^2 ≤ BMI < 29.9 kg/m^2), and obesity (BMI ≥ 30 kg/m^2). This classification reflects the purpose of this study to examine the factors that are associated with overweight and obesity. The BMI categories were then coded as 0 = underweight, 1 = normal weight, 2 = overweight, and 3 = obesity.

Social and demographic factors consisted of age, gender, race, and marital status. The age of the survey respondents was measured in years with a minimum of 18 years. The gender (sex) of the survey participants was classified into female (= 1, i.e. coded with 1) and male (= 2). Race was divided into Hispanic (= 1) and non-Hispanic (= 0). The non-Hispanic group was further divided into White (= 1), Black (= 2), Native Alaskan/Hawaii/Indian (= 3), and Asian (= 4). The marital status of the survey participants was classified as married (= 1), living with partner (= 2), widowed/divorced/separated (= 3), and never married (= 4).

Lifestyle variables included drinking (alcoholic consumption), smoking, sleep, and physical activity. Drinking was classified into former drinking (= 1), current frequent (= 2), current moderate (= 3), current heavier (= 4), and lifetime abstainer (= 5). Smoking was classified into current everyday (= 1), current someday (= 2), smoker (= 3), and never (= 4). Sleep was measured in number of hours, as a continuous variable.

Table 1. Selected NHIS variables included in this study, their coding and frequencies/means

Variable	Measurement	Frequency (%) or mean (st. dev.)
Dependent variable		
Body Mass Index (BMI)	Underweight = 0	1.7
	Normal weight = 1	34.8
	Overweight = 2	34.6
	Obese = 3	28.9
Independent variables		
Age	Years	M = 48.5 (18.2)
Sex	Female = 1	55.1
	Male = 2	44.9
Race[a] (non-Hispanic)	White = 1	76.4
	Black = 2	15.8
	Alaskan/Hawaii/Indian = 3	1.2
	Asian = 4	6.6
Hispanic	Yes = 1	16.9
	No = 2	83.1

Table 1. (continued)

Variable	Measurement	Frequency (%) or mean (st. dev.)
Marital status	Married = 1	43.3
	Living with partner = 2	6.2
	Widowed/divorced/separated = 3	26.5
	Never married = 4	24.0
Smoking	Current every day = 1	14.5
	Current someday = 2	4.2
	Former smoker = 3	22.2
	Never = 4	59.0
Drinking	Former drinking = 1	15.9
(alcoholic consumption)	Current infrequent = 2	42.4
	Current moderate = 3	14.7
	Current heavier = 4	5.3
	Lifetime abstainer = 5	21.7
Moderate activity	Per day = 1	15.5
	Per week = 2	40.0
	Per month = 3	2.7
	Per year = 4	0.6
	Unable to do it = 5	1.5
	Never = 6	39.7

Table 1. (continued)

Variable	Measurement	Frequency (%) or mean (st. dev.)
Vigorous activity	Per day = 1	7.0
	Per week = 2	33.2
	Per month = 3	3.0
	Per year = 4	0.7
	Unable to do it = 5	2.2
	Never = 6	53.9
Strength activity	Per day = 1	3.9
	Per week = 2	21.2
	Per month = 3	1.7
	Per year = 4	0.4
	Unable to do it = 5	1.6
	Never = 6	71.1
Sleep	Hours	7.2 (1.4)
Region of residency	Northeast = 1	16.7
	Midwest = 2	20.8
	South = 3	36.3
	West = 4	26.1

[a] The 2012 NHIS dataset employs the term *race*

Physical activity was represented by three levels of activity: moderate activity, vigorous activity, and strength activity. They were all classified into six categories: per day (= 1), per week (= 2), per month (= 3), per year (= 4), unable to do it (= 5), and never (= 6).

Region of residency was classified into Northeast (= 1), Midwest (= 2), South (= 3), and West (= 4). This variable was intended to represent the environment in different regions in the U.S.

3.2.4 Multinomial logistic regression modeling

BMI, an indicator of body fat content based on an individual's weight and height, has been widely used to measure underweight, healthy weight, overweight, and obese individuals in human populations. I used BMI as a proxy for weight status of individuals as it is a simple indicator of body fat content and a better measurement of body composition than weight alone (e.g., a short athlete may be overweight when considering weight alone, but have little body fat and large muscle mass).

As described earlier, I classified the weight status of the 34,525 people who responded to the 2012 NHIS into four distinct categories: underweight (BMI < 18.5 kg/m^2), normal weight (18.5 $kg/m^2 \leq$ BMI < 25 kg/m^2), overweight (25 $kg/m^2 \leq$ BMI < 30 kg/m^2), and obesity (BMI $\geq$ 30 kg/m^2). Because only a very small percentage (N = 587, about 1.7%) of respondents in the NHIS database were underweight (BMI <18.5 kg/m^2) and the underweight group was not a focus of this study, the underweight

category was not included in this analysis. In other words, I used only three BMI categories — normal weight, overweight, and obesity — in the statistical modeling.

Because I classified BMI into several categories for the purpose of this study, the weight status (BMI category) of an individual became a categorical variable. Given that linear regression is unable to handle a categorical dependent variable, I adopted multinomial logistic regression (MLR) for analysis. MLR is able to predict the relative probability of each category of the dependent or outcome variable (DV) based on multiple independent variables (IVs).

Additionally, the MLR model has several advantages. MLR does not require assumptions of normality, linearity, or homoscedasticity (Greene, 2012), representing an attractive and effective modeling tool. It is not only statistically robust but also attractive in risk analysis (Tabachnick & Fidell, 2013). In other words, the MLR model can portray the nonlinear relationship between independent variables and the dependent or outcome variable; the independent variables do not have to be continuous or unbounded; and the error term is not required to follow a normal distribution (Greene, 2012). Plus, nonlinear relationships do not follow a rule in which increases in one factor are always associated with corresponding, monotonic increases or decreases in the other factor. Because of these advantages, MLR modeling is especially suited for this study — to assess the statistical linkage between a set of SDELFs and BMIs categorized as normal weight, overweight and obese BMIs.

In the MLR model, I used normal weight or healthy weight as the reference category/variable. That is, the probability of being overweight or obese was modeled

relative to normal weight. MLR helped identify the factors that contribute to overweight and obesity relative to normal weight.

As discussed earlier (in Chapter 2), overweight and obesity can be attributed to demographic and socio-economic status and personal lifestyle (such as physical activity, drinking) among other factors. Drawing on these, it is assumed that the probability (P_{ij}) for individual *i* to be in weight status (or BMI category) *j* is a nonlinear function of various factors as follows:

$$P_{ij} = Pr(Y_i = j) = F(\boldsymbol{\beta}' \boldsymbol{X}_{ij}), \quad (1)$$

where $\mathbf{X}_{ij}$ is the vector of characteristics of individual *i* in weight status *j*, $\boldsymbol{\beta}$ is the vector of coefficients associated with $\mathbf{X}_{ij}$; *F* is the function notation; *Pr* denotes probability; and Y_i denotes the weight status of individual *i*.

Eqn. (1) is a nonlinear function, and its direct regression analysis is cumbersome. A common approach to handling a nonlinear function in regression modeling is to convert it to a linear function using a link function (association task) and then run the linear regression (Greene, 2012). Two widely-used link functions are the logistic distribution function (also called logit) and the normal distribution function. Because of its computational convenience when dealing with multinomial responses (Greene, 2012), the logit was used in this study. Hence, I applied the multinomial logit model to analyzing the factors that contribute to overweight and obesity. With the normalization of $\beta_r = 0$ (r being the reference response, normal weight), the model can be written as:

$$ln\left(\frac{P_{ij}}{P_{ir}}\right) = \boldsymbol{\beta}_j' \boldsymbol{X}_{ij}. \quad (2)$$

I adopted an interactive stepwise approach to empirically specify the multinomial logit model. This approach involved three major steps. First, I selected an array of independent variables that were likely to influence an individual's BMI. The description of these variables and their frequencies/mean are shown in Table 1. These variables range from socio-demographic characteristics (age, sex, race, and marital status) to environmental and lifestyle indicators (region of residency, alcohol consumption, physical activity, strength training, smoking, and hours of sleep). All these independent variables were included in the initial model. In the dataset, there was no information regarding income, and the only education data was whether an individual attended school in the past 12 months. Due to these data limitation, income and education could not be included in the model.

Second, I used the stepwise backward approach to eliminate statistically non-significant independent variables, one at a time, to derive a preliminary regression model. Independent variables were eliminated from the model based on a chi-square (Wald) statistic and its associated *p*-value; variables with the largest *p*-value were removed first. Any independent variables with a *p*-value greater than 0.10, were removed from analysis.

Third, the stepwise forward approach was employed to re-enter the previously eliminated independent variables, one by one, back into the model. If any independent variable had a *p*-value greater than 0.10, then the variable was removed; the remaining independent variables with a *p*-value smaller than 0.05 were kept in the model. Steps 2

and 3 were repeated iteratively until the model converged, which yielded the final regression model.

The final model was further validated using several statistical tests in addition to the chi-square test for significance of individual variables, including the log likelihood, likelihood ratio, and Wald tests (Greene, 2012). No evidence of multi-collinearity among the independent variables in the final model was found according to the variance inflation factor (VIF) and simple correlation coefficients. SPSS version 22 (Arbuckle, 2013) was used in the modeling.

3.3 Results

3.3.1 Descriptive statistics

Among the 34,525 NHIS participants in 2012, 34.7% had normal weight, 28.9% were obese, and another 34.6% were overweight. This suggests that almost two-thirds of the U.S. adult population had a BMI above the normal weight.

The age of the survey participants ranged from 18 to over 85 years with a mode of 48.0, a mean of 48.5, and a standard deviation of 18.2. Females constituted 55.1% of the survey sample. Nearly 17% of the sample were Hispanic, and some 83% were non-Hispanic. Among the non-Hispanic, 76.4% were Whites, 15.8% were Blacks, 6.6% were Asians, and 1.2% were Native Alaskans/Hawaii/Indians. Less than a quarter (24%) of the sample was never married, 43.3% were married, 6.2% lived with a partner, and 26.5% were widowed/divorced/separated.

Less than one-fourth of the sample (21.7%) never drank (alcoholic consumption), while 15.9% were former drinkers, 42.4% were current infrequent drinkers, 14.7% were current moderate drinkers, and 5.3% were current heavier drinkers. Compared to drinking, fewer survey participants smoked. Fifty-nine percent (59%) never smoked, 14.5% were current everyday smokers, 4.2% were current occasional smokers, and 22.2% were former smokers. On average, the survey participants slept 7.2 hours per day.

Most of the survey respondents participated in *moderate* physical activity with 39.7% declaring they had never participated in any. Nearly 16% (15.9%) of them engaged in moderate activity every day, 40% did so each week, 2.7% did each month, 0.6% each year, and 1.5% were unable to engage in moderate physical activity.

Almost 54% (53.9%) never participated in *vigorous* physical activity. Few (2.2%) were unable to do it; 0.7%, 33.2%, 0.3%, and 0.7% of participants engaged in vigorous physical activity on a daily, weekly, monthly, and yearly basis, respectively.

Of the three levels of physical activity (moderate, vigorous, and strength activity), strength activity was the least popular among the survey participants. Over 70% (71.1%) of them never engaged in strength training, and 1.6% were unable to do so. Those participating in strength activity on a daily, weekly, monthly, and yearly basis constituted 3.9%, 21.2%, 1.7%, and 0.4% of the sample, respectively.

The regional (geographic) distribution of survey participants yielded 16.7% in the Northeast, 20.8% in the Midwest, 36.3% in the South, and 26.1% in the Western U.S.

3.3.2 Multinomial logistic regression results

The final MLR models (Table 2) underwent several statistical tests. The likelihood ratio and Pearson chi-square tests indicated that the independent variables (SDLEFs) were jointly significant ($p < 0.05$) in predicting the log odds ratio of being overweight or obese vs. being normal weight, for the U.S. adults included in the 2012 NHIS. All statements on statistical significance in this section are based on a 5% significance level if not otherwise noted.

In this sample, age is a statistically significant predictor of overweight but not obesity. Controlling for all other variables, the multinomial logit (log odds ratio) of being overweight relative to normal weight for the adults participating in the 2012 NHIS increases by 0.01 with a one-year increase in age. Correspondingly, the odds ratio (OR) of overweight vs. normal weight is 1.01 for age. This small odds ratio is because of the small increment (1 year) between two adjacent age groups.

Gender (sex) is significantly associated with both overweight and obesity. After controlling for multiple variables, women are more likely than men to be overweight or obese relative to normal weight. In terms of gender (female vs. male), the odds ratio is 2.25 for being overweight relative to normal weight and 1.56 for being obese relative to normal weight. The women in this sample, therefore, were twice as likely to be overweight as men, and 56% more likely to be obese.

Table 2. Maximum likelihood estimates of a multinomial regression model assessing the relationship between various socio-demographic, lifestyle, and environmental factors and the probability of U.S. adults being overweight or obese

Parameter[a]	Category or unit	Overweight vs. normal weight				Obesity vs. normal weight			
		Estimated β	Odds ratio	Wald χ^2	*p*-value	Estimated β	Odds ratio	Wald χ^2	*p*-value
Intercept		-1.37		170.46	.000	-1.35		123.81	.000
Age	Years	.01	1.01	69.40	.000	.00	1.00	0.01	.940
Sex	Female	.81	2.25	755.67	.000	.45	1.56	201.94	.000
	Male[b]								
Race	White	.64	1.90	131.95	.000	1.55	4.70	372.86	.000
	Black	1.05	2.86	255.07	.000	2.19	8.94	635.70	.000
	Alaskan/Hawaii/Indian	1.01	2.73	47.03	.000	2.13	8.42	185.83	.000
	Asian[b]								
Hispanic	Yes	.36	1.43	77.66	.000	.31	1.36	52.71	.000
	No[b]								

Table 2. (continued)

Parameter[a]	Category or unit	Overweight vs. normal weight				Obesity vs. normal weight			
		Estimated β	Odds ratio	Wald χ^2	*p*-value	Estimated β	Odds ratio	Wald χ^2	*p*-value
Marital status	Married	.40	1.49	107.39	.000	.33	1.39	65.85	.000
	Living with partner	.24	1.28	14.95	.000	.15	1.16	4.96	.026
	Widowed/divorced/separated	.26	1.30	31.67	.000	.19	1.21	16.07	.000
	Never married[b]								
Smoking	Current daily	-.24	.79	30.18	.000	-.27	.76	37.32	.000
	Current someday	-.01	.99	.02	.877	-.06	.94	.62	.433
	Former smoker	.11	1.12	8.99	.003	.26	1.30	43.48	.000
	Never[b]								
Drinking	Former drinking	.13	1.13	6.63	.010	.23	1.26	21.44	.000
	Current infrequent	.11	1.12	8.33	.004	.17	1.19	17.60	.000
	Current moderate	.02	1.02	.10	.758	-.22	.81	15.56	.000

Table 2. (continued)

Parameter[a]	Category or unit	Overweight vs. normal weight				Obesity vs. normal weight			
		Estimated β	Odds ratio	Wald χ^2	*p*-value	Estimated β	Odds ratio	Wald χ^2	*p*-value
	Current heavier	-.03	.97	.24	.627	-.27	.77	12.18	.000
	Lifetime abstainer[b]								
Moderate activity	Per day	-.07	.93	2.23	.136	-.08	.92	2.84	.092
	Per week	-.05	.95	1.78	.182	-.01	.99	.03	.866
	Per month	-.27	.76	8.24	.004	-.06	.94	.42	.519
	Per year	-.15	.86	.65	.420	-.13	.88	.42	.515
	Unable to do it	-.14	.87	.33	.567	-.22	.81	.87	.351
	Never[b]								
Vigorous activity	Per day	-.14	.87	5.25	.022	-.36	.70	28.73	.000
	Per week	-.10	.91	6.93	.008	-.32	.73	66.51	.000
	Per month	.21	1.24	5.90	.015	.00	1.00	.01	.967

Table 2. (continued)

Parameter[a]	Category or unit	Overweight vs. normal weight				Obesity vs. normal weight			
		Estimated β	Odds ratio	Wald χ^2	*p*-value	Estimated β	Odds ratio	Wald χ^2	*p*-value
	Per year	.10	1.10	.31	.578	.18	1.20	.23	.635
	Unable to do it	.08	1.08	.18	.670	.48	1.61	7.13	.008
	Never[b]								
Strength activity	Per day	-.16	.85	4.82	.028	-.50	.61	35.09	.000
	Per week	-.18	.84	22.37	.000	-.60	.55	195.83	.000
	Per month	.01	1.01	.01	.957	-.54	.58	19.17	.000
	Per year	-.39	.68	3.60	.058	-.73	.48	9.67	.002
	Unable to do it	.14	1.15	.45	.504	.02	1.02	.01	.931
	Never[b]								
Sleep	Hours	-.05	.95	26.04	.000	-.10	.91	86.12	.000

Table 2. (continued)

Parameter[a]	Category or unit	Overweight vs. normal weight				Obesity vs. normal weight			
		Estimated β	Odds ratio	Wald χ^2	*p*-value	Estimated β	Odds ratio	Wald χ^2	*p*-value
Region	Northeast	-.04	.96	.93	.335	-.09	.92	3.37	.066
	Midwest	.07	1.07	2.91	.088	.19	1.21	18.92	.000
	South	.04	1.04	1.22	.270	.09	1.09	5.13	.024
	West[b]								
-2 log likelihood (intercept and covariates)		69324.06							
Likelihood ratio (chi-square)		3621.13 (*p*=0.000)							
Pearson (goodness-of-fit)		92685.13 (*p*=0.029)							

[a] Only the independent variables with a *p*-value < 0.05 are listed.

[b] The reference category used in the multinomial regression model.

In terms of race, overweight and obesity are more likely to be observed among Hispanic than among non-Hispanic adults. The odds ratio of overweight relative to normal weight is 1.43; the OR for obesity is 1.36 for Hispanics when compared to non-Hispanics. Among non-Hispanic adults, Asians have a much lower risk of overweight or obesity relative to normal weight than Whites, Blacks, or Native Alaskans/Hawaii/Indians. Compared to Asians, the odds ratio of being overweight (or obese) relative to normal weight is 1.90 (OR for obesity = 4.70) for Whites, 2.86 (OR for obesity = 8.94) for Blacks, and 2.73 (obesity OR = 8.42) for Native Alaskans/Hawaii/Indians, respectively. In other words, after controlling for multiple factors, compared to Asians the risk of being overweight (obese) relative to normal weight increases by a factor of 1.90 (4.70) for Whites, by a factor of 2.86 (8.94) for Blacks, and by a factor of 2.73 (8.42) for Native Alaskans/Hawaii/Indians.

Marital status was found to be significantly correlated with overweight and obesity as well. Compared to those "never married," the odds ratio of overweight (obesity) relative to normal weight was 1.49 (1.39) for "married," 1.28 (1.16) for "living with partner," and 1.30 (1.21) for "widowed/divorced/separated," respectively. This implies that the likelihood of being overweight or obese relative to normal weight is lower in adults who have never married than in any other group, if all other factors are held constant.

Smoking, too, was significantly associated with overweight and obesity in this sample. Interestingly, current everyday smokers were less likely to be overweight or obese than those who never smoked, but former smokers are more likely to be

overweight or obese than those who never smoked. Compared to adults who never smoked, the odds ratio of overweight (obesity) vs. normal weight is 0.79 (0.76) for current everyday smokers and 1.12 (1.30) for former smokers. The odds ratios are not significantly different between current someday smokers and those who never smoked. This distribution of findings suggests that those who smoked and then quit tend to have a higher risk of being overweight and obese than those who never smoked or currently smoke every day.

The statistical relationship between drinking (alcohol consumption) and weight status also was significant. Former drinkers and current infrequent drinkers seem more likely to be overweight or obese than lifetime abstainers whereas current moderate and heavier drinkers are less likely to be obese than lifetime abstainers. Compared to lifetime abstainers, the odds ratio of overweight (obesity) relative to normal weight is 1.13 (1.26) for former drinkers and 1.12 (1.19) for current infrequent drinkers. On the other hand, the odds ratios of overweight relative to normal weight are not significantly different between lifetime abstainers and current moderate or heavier drinkers. The odds ratio of obesity relative to normal weight for current moderate or heavier drinkers is significantly different from that for lifetime abstainers. Compared to lifetime abstainers, the odds ratio of being obese is 0.81 for current moderate drinkers and 0.77 for current heavier drinkers. Therefore, holding all other factors constant, current moderate and heavier drinkers are less likely to be obese than lifetime abstainers.

The statistical association between physical activity and weight status varied with the type of activity. In general, physical activity is negatively related to overweight or

obesity, and the magnitude of the association increases with a rise in the frequency of physical activity. Of the three types of physical activity, moderate activity appears to have the smallest correlation with overweight or obesity, and strength activity has the strongest association.

Moderate physical activity has no significant correlation with obesity, and only moderate physical activity *on a monthly basis* is significantly and negatively correlated with overweight.

Vigorous physical activity on a daily or weekly basis, however, is significantly associated with both overweight and obesity. Compared to those who never participate in vigorous activity, the odds ratio of overweight (obesity) relative to normal weight is 0.87 (0.70) for those engaging in daily vigorous activity and 0.91 (0.73) for those participating in weekly vigorous activity. This implies that daily vigorous activity can reduce the risk of overweight (obesity) relative to normal weight by a factor of 0.87 (0.70), and that weekly vigorous activity can reduce the risk of overweight (obesity) relative to normal weight by a factor of 0.91 (0.73) if all other factors remain constant.

Strength training activity, among this sample, shows strong correlations with weight status, particularly with obesity — *regardless of the frequency of the activity*. Only daily and weekly strength building is significantly and negatively correlated with overweight, but strength training on a daily, weekly, monthly, or even yearly basis shows significant and negative associations with obesity. Interestingly, the frequency of participating in strength activity does not seem to affect the odds ratio of obesity or overweight relative to normal weight. Daily or weekly strength activity can reduce the

risk of overweight relative to normal weight by a factor of approximately 0.85, and participating in strength activity daily, weekly, or monthly can reduce the risk of obesity relative to normal weight by a factor between 0.55 and 0.61 if all other variables remain constant. Therefore, participation in strength-building physical activity, even on an infrequent basis, seems more helpful in reducing the risk of obesity than engaging in moderate or infrequent vigorous physical activity.

Hours of sleep also revealed a significant and negative correlation with overweight or obesity. For every additional hour of sleep, for this sample, log odds ratios reduced by 0.05 for overweight relative to normal weight and by 0.10 for obesity relative to normal weight, respectively. If all other factors remain constant, the risk of being overweight or obese relative to normal weight decreases as one sleeps more.

There were no statistically significant regional differences in the odds ratios of *overweight* relative to normal weight among the adults participating in the 2012 NHIS. Yet, adults residing in the Midwest and the South were more likely to be *obese* than those in the West, with an odds ratio of 1.21 for the Midwest and 1.09 for the South, relative to the West.

3.4 Discussion

3.4.1 Health disparities in overweight and obesity

This study revealed that disproportional overweight and obesity risks exist in different age, racial, and sex/gender groups as the odds ratios are statistically different across the different levels or categories of these demographic independent variables

(Table 2). Several aspects of my findings related to disparities in overweight and obesity echo the results of previous studies (McLaren, 2007; Wang & Beydoun, 2007; Zhang & Wang, 2004a & 2004b); however, these studies emphasized socioeconomic *differences* (SES). For instance, Mclaren (2007) found a positive relationship between socioeconomic status and obesity for both men and women. Wang and Beydoun (2007) reported that minorities including non-Hispanic Black men, Hispanic women, and Native Americans had a higher obesity rate than Whites and Asians, and that Asians had the lowest obesity rate. Using the data from the National Health and Nutrition Examination Survey III, 1988-1994 (NHANES III) among adults aged 18-65 years, Zhang and Wang (2004a) adopted the Concentration Index (CI) to assess socioeconomic inequality in obesity across age, gender, and ethnic groups and found that these factors could be important in explaining the inequality in obesity.

The findings from this study are also in line with the obesity trends from the latest obesity statistics and reports. A recent report by the Trust for America's Health and the Robert Wood Johnson Foundation (2014), based on the data from the Behavioral Risk Factor Surveillance System, indicates that the obesity rate of African American adults is nearly 1.5 times that of White adults, and 42.5% of Latino adults are obese compared to 32.6% of Whites. Additionally, 76.2% of Blacks and 77.9% of Latinos are overweight compared to 67.2% of White adults in the same BMI category. The latest annual report of the Trust for America's Health and the Robert Wood Johnson Foundation (2017) showed that obesity rates are the highest among middle aged adults (40 to 59 years) compared to the younger group (20 to 39 years) and to older adults (≥

60 years). The obesity rate in the middle age group was 41.0% compared to 34.4% in the younger group and 38.5% in the older group in 2011-2014, in that report. The findings of these reports support my result that the overweight and obesity risk varies with age and differs across gender and racial groups.

Despite the statistical evidence and the findings from several studies about the disproportional overweight and obesity rates among minorities, the underlying mechanisms or pathways related to this health disparity are largely unknown. To search for answers, Adler and Stewart (2010) suggest moving from description to "exploration of pathways" with "a focus on interactions among factors, not just their main effects or contributions as mediators," (p. 1). This study points to the strong evidence of disparities in overweight and obesity risk across demographic groups, suggesting the need to address this disparity problem. Given the complex connectivity between overweight/obesity and influencing factors, the above call for new research to explore the depth and complexity of this health disparity seems necessary.

The health disparity and inequality in overweight and obesity requires that health educators and designers of public health programs pay closer attention to vulnerable minority groups. The nonlinear relationships among age, gender, race/ethnicity, and BMIs add challenges to addressing the overweight and obesity issue, and explains why the piecemeal approach and the "one size fits all" formula for prevention and intervention programs has not been successful (Chan & Woo, 2010; Foster et al., 2003; Kristeller & Hoerr, 1997; Roberto et al., 2015; Seburg, Olson-Bullis, Bredeson, Hayes, & Sherwood, 2015; Taveras et al., 2011). The high overweight and obesity risk among

Hispanics and Blacks in the U.S. needs special attention, particularly as these racial/ethnic groups are becoming a larger portion of the U.S. population. Nearly one in four (24.8%) women are obese before becoming pregnant in 2014 (Branum, Kirmeyer, & Gregory, 2016), which can increase risk to the new born and alter the child's susceptibility to develop obesity later in life. All these nuances call for more innovative, integrative, and effective health education and intervention programs tailored for specific age, gender, and racial/ethnic groups.

3.4.2 Strength training vs. other physical activity

The results from this study provide strong statistical evidence suggesting that both strength and resistance training are more effective in reducing the risk of overweight and obesity than moderate or even vigorous physical activity. The MLR modeling results show that strength training or resistance training is the factor exhibiting the strongest negative/inverse association with overweight and obese BMIs. Strength training shows robust results across all regression models, regardless of joint or separate considerations of the SDELFs. Of the three types of physical activity examined, strength training activity displays the strongest negative relationship with the risk of overweight and obesity, followed by vigorous activity for overweight and obesity, and moderate physical activity for overweight only (no relationship with obesity).

Contrary to conventional wisdom, several recent clinical studies also indicate that strength training is more effective in reducing the percentage of body fat than aerobic exercise (Schmitz et al., 2007), and can better reduce body weight, compared to aerobic

or other exercise (Bloomer, 2005). The efficacy of strength building in reducing body fat may be partly due to increases in the resting metabolic rate, total energy expenditure, and oxygen consumption after strength activity (Ades et al., 2005; Aristizabal et al., 2015; Kirk et al., 2009; da Mota et al., 2010).

Despite the benefit of strength training for mitigating overweight and obesity risk, a large portion of U.S. adults have not participated in strength training or in any other physical activity, according to this study's findings. According to the State of Obesity report (the Trust for America's Health and the Robert Wood Johnson Foundation, 2017), 80% of American adults do not meet the government-recommended national physical activity prescription (150 minutes per week of moderate physical activity for normal weight adults) for aerobic and muscle strengthening. The descriptive statistics of the data used in this study indicate almost 70% of U.S. adults either never participated in strength or vigorous physical activity or were unable to do so. Physical inactivity cost $27.8 billion in the U.S. in 2013, of which $24.7 billion was direct health care costs and the remaining $3.1 billion was the associated productivity loss (Ding et al., 2016).

Given the statistically significant association between strength training activity and reduced BMI found in this study's statistical models, strength building activity can be an important element in combating overweight and obesity. Strength training can be incorporated into high school and college physical education courses and public health education programs. However, other physical activity (e.g., moderate and vigorous activity) should not be ignored as it can lead to other health benefits; in terms of weight

control, however, the data used in this study strongly support the role of strength training over and beyond other types of activity. Strength building activity should, therefore, be combined with aerobic exercise and diet in order to achieve overall health benefits including weight control (da Mota et al., 2010).

3.4.3 Epigenetic factors

Most of the SDELFs examined in this study are more closely related to external environmental or epigenetic (nurture) factors than to internal biological or genetic phenomena (nature). For instance, lifestyle factors such as smoking, drinking, marital status, and hours of sleep are all associated with overweight and obese BMIs, though via different mechanisms. The geographic or regional differences in weight status also suggest the possible influence of external factors. Gender and race are related to genetics, but their heterogeneous associations with overweight and obesity risk may be due to their interactions with epigenetic causes, which warrants further investigation. Overall, the data used in this study indicate that epigenetic factors may be playing a critical role in shaping the weight status of U.S. adults although the role that genetics may also play should not be underestimated.

Other research and clinical studies have also revealed the linkage between epigenetic factors and overweight or obesity. Dolinoy et al. (2006) studied genetically identical mice and fed them with different diets. They found that, for the mice fed with a methyl rich diet, a specific region of their DNA became hyper-methylated and their agouti coat gene, which regulates the pigment distribution in a mammal's coat, was

"turned off." On the other hand, for the mice fed with a methyl poor diet, their agouti gene was hypo-methylated or "turned on." Turning "on" or "off" the agouti gene altered not only the mice's coat color but also their genetic propensity to obesity, T2D, and many other metabolic diseases, clearly pointing to the effects of diet in causing these outcomes. Similarly, Ling, Kelechi, Mueller, Brotherton, and Smith (2012) monitored a group of men six months after regular spinning and aerobics exercise and found that epigenetic changes had taken place in 7,000 genes (an individual has over 200 different types of cells and each cell has 20,000-25,000 genes). They also found that physical activity altered the DNA methylation in genes which are linked to obesity and T2D in fat cells (for a more detailed discussion on this including other animal and human studies, see Chapter 2, section 2.3.1).

This study points to the necessity and importance of health education and health interventions that target epigenetic factors alongside genetic and other factors. This integration, no doubt, highlights the complexity of the overweight and obesity issue, but it supports the notion that health education and intervention programs that address socio-demographic, lifestyle, physical activity, and environmental conditions of individuals, *simultaneously*, can be more effective than programs targeting one or two factors in isolation.

3.4.4 Strengths and limitations of this study and future directions

Strengths

In contrast to many studies, this study examined a nationally-representative sample of adults in the U.S., covering a wide range of ages (from18 to 86 years) and assessing both males and females, most racial/ethnic groups, and all geographic regions in the United States. I used Body Mass Index (BMI), a simple and useful indicator (based on weight and height), widely used around the world to gauge body weight and the risk of certain diseases associated with overweight and obesity. According to the World Health Organization's BMI classification, I further classified BMI into: normal weight (BMI = 18.8-24.9 kg/m^2), overweight (BMI = 25-29.9 kg/m^2), obesity (BMI $\geq$ 30 kg/m^2), and underweight (BMI < 18.8 kg/m^2) (underweight was excluded from this analysis).

Another strength of this study is the application of a systematic approach to understanding the complexity of the obesity crisis. I included a wide range of socio-demographic, environmental, and lifestyle factors (SDELFs) and assessed their effects, simultaneously. Using normal weight as the reference, I used the multinomial logistic regression modeling approach to statistically link the risk of overweight and obesity to the array of SDELFs. This nonlinear modeling approach compares overweight and obesity to normal weight and takes into account, simultaneously, multiple SDELFs (independent variables) that are potentially related to overweight and obesity. Unlike a piecemeal modeling method or a simple bi-variate analyses, I considered multiple body weight statuses and multiple SDELFs together. As such, this study is more

comprehensive, and its nonlinear approach better reflects the complex web of connectivity between body weight and SDELFs. To the best of my knowledge, this study is among the first few that have applied MLR modeling to simultaneously compare multi-levels of weight status or BMIs (overweight and obesity vs. normal weight) in a context of jointly considering an array of factors (independent variables), the SDELFs.

Limitations

Despite its strengths, this study has limitations. Data for all variables including BMI in the NHIS 2012 dataset were based on self-reporting or recalled information collected through in-house surveys, which might not be as accurate as standardized measures of these variables would have been. For example, self-reported BMI could have underestimated body fat for those who have lost muscle mass (e.g., older people) and overestimated body fat for those who have built muscle mass (e.g., athletes). The same issue of self-reporting for the SDELFs could have represented a limitation in this study.

Previous studies have shown that men are more likely to overestimate their height regardless of their age, and older women are more likely to overestimate their height compared to younger women (Merrill & Richardson, 2009). Adult weight tends to be underestimated by women (by as much as 0.85 kg) more than by men (0.54 kg), and women seem to overestimate height (0.40 cm) more than men (0.38 cm) (Niedhammer, Bugel, Bonenfant, Goldberg, & Leclerc, 2000). Additionally, the degree of variation related to BMI bias can vary by up to plus or minus 2 BMI units

(Niedhammer et al., 2000). However, this self-reporting bias was mitigated in this study as overweight and obesity were analyzed relative to normal weight using multinomial logistic regression. In other words, the odds ratios derived from the nonlinear multinomial logistic regression technique corrected for the potential BMI self-reporting bias as long as the self-reporting biases were consistent.

Finally, income and education are likely to be associated with overweight and obesity. However, because there was no information on income and inadequate information on education in the NIHS dataset, income and education of the survey participants could not be included in this study.

Future directions

This study's findings have important implications for future health research, education, and intervention programs aimed at mitigating the overweight and obesity epidemic:

1) Health promotion scholars should adopt nonlinear and holistic approaches to research and program development

Many current overweight and obesity intervention programs are narrowly focused on a single or few variables/factors. This piece-meal approach has proven to have limited effectiveness (Chan & Woo, 2010; Roberto et al., 2015). Overweight and obesity interventions need to include multiple variables associated with socioeconomic, demographic, nutrition, lifestyle, environmental, genetic, and epigenetic factors and to aim at intermediate- and long-term programs. The sociodemographic, environmental,

lifestyle factors/variables, and BMIs are not associated in an isolated and simple linear relationship. In other words, they exert joint effects, synergistically — yielding outcomes that are, always, greater than the sum of the factors. Therefore, when health educators design obesity intervention programs, they need to consider that age, ethnicity, gender, and the environment all interact and shape lifestyles which, in turn, affect people's weight and overall health.

2) Health promotion scholars should recognize and address the disparities in overweight and obesity across ethnic and gender groups

There are disparities in overweight and obesity risk across age, racial/ethnic, and gender groups. This disparity problem needs to be addressed in order to tackle the national obesity crisis. Addressing the disparities entails an in-depth understanding of their causes. Such an understanding will help develop and implement education and intervention programs targeting those with high risk of overweight and obesity. Additional comparative studies of different socio-demographic groups would also be helpful. Moreover, health education, promotion, and intervention programs should pay more attention to these high-risk groups.

Future research can explore the disparities by incorporating income and education levels into analyses. Such research could shed new light on the overweight and obesity crisis and the possible connectivity between overweight/obesity (a health issue) and some socio-economic challenges.

3) Future research should focus on extending this study by applying the modeling strategy used herein to other public health concerns

The MLR modeling approach used in this study can be used to examine other health issues, such as chronic diseases including cardiovascular diseases and cancers. This nonlinear modeling approach does not assume that the dependent variable always changes proportionally with an independent variable, thus better reflecting the real-world scenarios (Chan & Woo, 2010; Roberto et al., 2015; Wang et al., 2013). Meanwhile, the model and analysis can be updated as more and new data from various sources become available and can be combined.

In summary, this study helps inform future health education and associated research efforts of the importance of considering nonlinear, integrative, and holistic approaches to both understanding and addressing health disparities associated with overweight/obesity. Taking into account the joint nonlinear effects of multiple lifestyle and environmental factors, while addressing inherent disparities, represents both a challenge and an opportunity for health researchers, educators, and practitioners who search for solutions to the overweight and obesity epidemic in the U.S. and world-wide.

4. OVERALL SUMMARY AND CONCLUSIONS

This study has fulfilled two major objectives: 1) to explore the importance of and potential for incorporating epigenetics approaches into health education and interventions to mitigate overweight and obesity; and 2) to quantify the statistical relationship between body mass index (BMI) and a set of socio-demographic, environmental, and lifestyle factors (SDELFs) in a representative sample of U.S. adults. The first objective was achieved via a review and synthesis of existing literature, and the second objective was accomplished via multinomial logistic regression analysis.

Recent advances in genetics, genomics, epigenetics, and health sciences, alongside with empirical evidence, point to the complexity of the overweight and obesity problem. Approaches based on genetics alone cannot explain or resolve the overweight and obesity epidemic, and gene-environment interactions are increasingly recognized as an important or even dominant reason behind overweight and obesity (Harvard School of Public Health, 2017; Qi & Cho, 2008; Reddon et al., 2016). Many SDELFs play a role in developing overweight and obesity, and their roles are intertwined. Epigenetic influences can have long-lasting effects and can pass onto subsequent generations (Grossniklaus, Kelly, Ferguson-Smith, Pembrey, & Lindquist, 2013; Saey, 2013). All these indicate the necessity and benefits to adopt epigenetic principles and mechanisms in preventing and controlling overweight and obesity.

The 2012 NHIS data (N = 34,525) of U.S. adults were used to assess the linkage between a set of SDELFs and body mass index (BMI). BMI in this study was classified

into four categories: underweight, normal weight, overweight, and obese. The underweight category was not analyzed in this study given its small frequency and the inquiry's focus. A multinomial logistic regression (MLR) model was used to estimate the statistical relationship between the obese/overweight BMI categories (setting normal weight BMI as the reference group) and a set of 12 SDELFs (independent variables). The regression modeling revealed that non-genetic factors such as the SDELFs assessed were statistically significantly associated with overweight and obesity among U.S. adults. Age, sex, race/ethnicity, marital status, hours of sleep, smoking, drinking, region of residence, and physical activity all exhibited associations with overweight and obesity (BMI). However, these associations were nonlinear and, in most cases, non-monotonic (not always in one direction). Additionally, overweight and obesity risks were also found to be significantly different across age, racial/ethnic and gender groups, and geographic regions in this study's sample.

These findings have several important implications for health education and interventions as well as for research aimed at understanding and resolving the overweight and obesity issue. First, the factors associated with overweight and obesity are many, and the relationships among these factors and overweight or obesity are complex. This multi-factorial relationship may explain why the past linear and piecemeal approaches in health education and promotion have not been successful in preventing and controlling overweight and obesity. Meanwhile, the complex relationships among multiple variables call for multidisciplinary and more holistic approaches to dissect the causes of the overweight and obesity epidemic and resolve it.

For a long time, public perception has favored genetics as the answer to most health and morbidity matters. This perception needs to change. Genetic factors should not be blamed for overweight and obesity or considered a barrier to improving the weight status of any individual or population. Furthermore, it is almost impossible to change our genome and genetic makeup. Although it has been reported that scientists would be able to apply CRISPR-Cas9, a technique developed by researchers at MIT, Harvard, Berkeley, and elsewhere over the last several years, to make precise changes to the genome to correct a single mutation (akin to molecular scissors for genome surgery) (Ran et al., 2013), obesity is associated with dozens or hundreds of genes and thus difficult to be regulated via genetic engineering approaches.

Epigenetics can play an important role in future health education and intervention programs aimed at preventing and reducing overweight and obesity given the associations of lifestyle and environmental factors with epigenetic mechanisms (see Chapter 2). Assisting individuals in initiating and sustaining lifestyle changes that can influence epigenetic fitness, seems practical and helpful given the limited capacity for changing genetic factors.

Based on the 2012 NHIS sample and MLR results, the disparities in risk for overweight and obesity occurring across different age, gender and racial/ethnic groups and geographic regions also indicate that a one-size-fits-all method or program might not work in addressing the national (and international) overweight and obesity issue. Future health education and intervention programs need to pay more attention to the higher

overweight and obesity rates among African-Americans and Hispanic-Americans in addressing these disparities.

The nonlinear and non-monotonic relationships among the SDELFs and overweight/obesity risk further suggest that it is challenging to understand and address the complex dynamics surrounding the overweight and obesity epidemic. A more in-depth understanding of this epidemic will entail innovative, broader, and long-term research that will help develop more effective health education and intervention programs. At the same time, health educators and public health professionals should be mindful that programs change over time and, if not updated, can become obsolete. Therefore, professionals should strive to continually incorporate new knowledge generated from research and clinical practice — as in the case of epigenetics knowledge.

In summary, there is no silver bullet or a single method to resolve the overweight and obesity epidemic. The complexity of the issue creates both challenges and opportunities for the field of health education and health promotion. Health educators and public health professionals can embrace the opportunity to advance their field and help resolve the issue by incorporating advancements in genetics, epigenetics, and health sciences into program design and implementation.

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